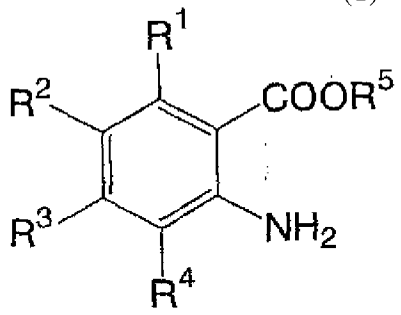
WO 03/064399 English Translation

CLAIM + DETAILED DESCRIPTION

[Claim(s)]

[Claim 1]

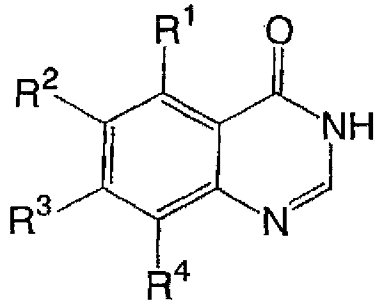
Formula (1) :



(1)

Among [type, R1, R2, R3, and R4 may be the same or different, respectively, and show the basis which does not participate in the following reaction. In addition, it may combine with each other and R1, R2, R3, and R4 may form the ring. R5 shows a hydrogen atom or a hydrocarbon group.]

Formula (2) characterized by coming out and making the anthranilic acid derivative shown and a Gyi acid derivative react under existence of carboxylic acid ammonium :



(2)

R1, R2, R3, and R4 are synonymous with the above among [type.]

The manufacture method of the quinazoline 4-ON derivative come out of and shown.

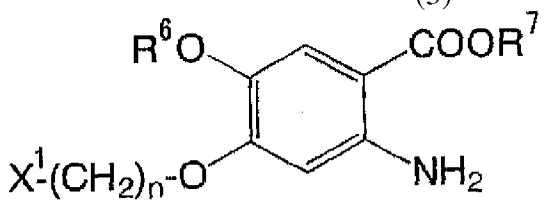
[Claim 2]

The manufacture method given in the claim 1 whose Gyi acid derivative is ORUTOGI acid ester.

[Claim 3]

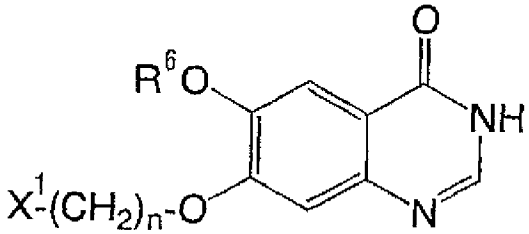
Each of R1, R2, R3, and R4 independently A hydrogen atom, an alkyl group, A cycloalkyl machine, an ARARUKIRU machine, an aryl group, a halogen atom, a hydronalium KISHIRU machine, It is the manufacture method given in the claim 1 which is an alkoxyl group, an ARUKIRUCHIO machine, a nitro group, a cyano group, a carbonyl group, an amino group, or a carboxyl group, whose R1 is not an amino group

and [whose R4 however, is not a carboxyl group].
[Claim 4]
Formula (3) :



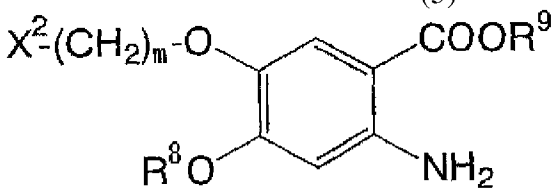
(3)

R6 shows an alkyl group among [type, R7 shows a hydrogen atom or a hydrocarbon group, and X1 shows a halogen atom. n shows the integer of 2-4.]
Formula (4) characterized by coming out and making the 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative shown and a Gyi acid derivative react under existence of carboxylic acid ammonium :



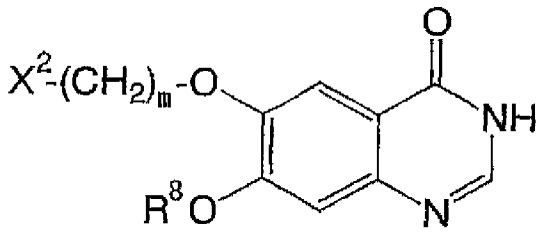
(4)

R6, X1, and n are synonymous with the above among [type.]
The process of the 6-alkoxy 7-halogeno alkoxy quinazoline 4-ON which comes out and follows the claim 1 shown.
[Claim 5]
A process given in the claim 4 whose Gyi acid derivative is ORUTOGI acid ester.
[Claim 6]
Formula (5) :



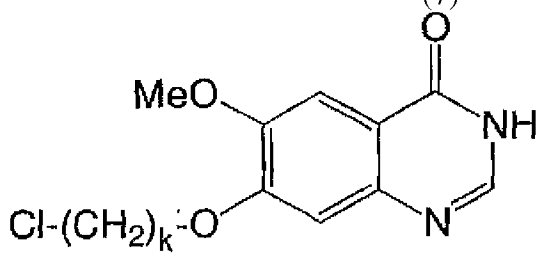
(5)

R8 shows an alkyl group among [type, R9 shows a hydrogen atom or a hydrocarbon group, and X2 shows a halogen atom. m shows the integer of 2-4.]
Formula (6) characterized by coming out and making the 4-alkoxy 5-halogeno alkoxy anthranilic acid derivative shown and a Gyi acid derivative react under existence of carboxylic acid ammonium :



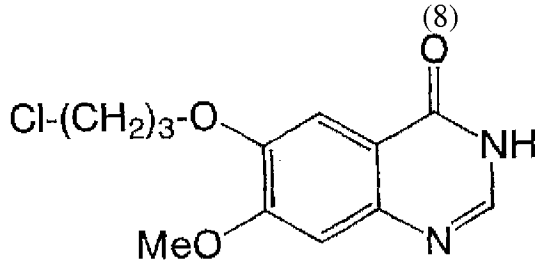
(6)

R8, X2, and m are synonymous with the above among [type.]
The process of the 7-alkoxy 6-halogeno alkoxy quinazoline 4-ON which comes out and follows the claim 1 shown.
[Claim 7]
A process given in the claim 6 whose Gyi acid derivative is ORUTOGI acid ester.
[Claim 8]
Formula (7) :



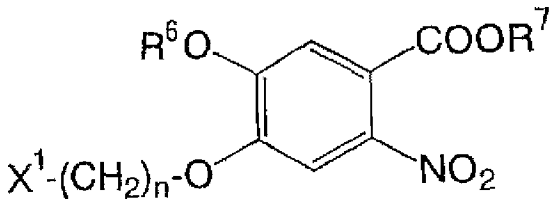
(7)

Me shows a methyl group among [type and k shows the integer of 2-4.]
6-********- 7-(3-chloro alkoxy) quinazoline 4-ON come out of and shown.
[Claim 9]
Formula (8) :



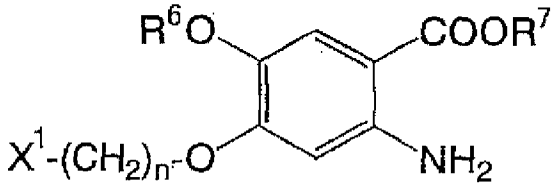
(8)

Me shows a methyl group among [type.]
7-********- 6-(3-chloro propoxy) quinazoline 4-ON come out of and shown.
[Claim 10]
Formula (9) :



(9)

R6 shows an alkyl group among [type, R7 shows a hydrogen atom or a hydrocarbon group, and X1 shows a halogen atom. n shows the integer of 2-4.] Formula (3) characterized by coming out and returning the 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative shown :



(3)

R6, R7, X1, and n are synonymous with the above among [type.] The process of the 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative come out of and shown.

[Claim 11]

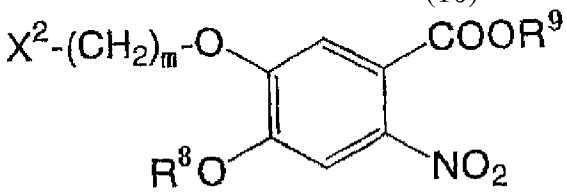
A process given in the claim 10 which performs the above-mentioned reduction under hydrogen atmosphere or Gyi acid existence under existence of a metal catalyst.

[Claim 12]

A process given in the claim 11 whose metal catalyst is the thing which is chosen from the group which consists of palladium, platinum, and nickel, and which contains one metal atom at least.

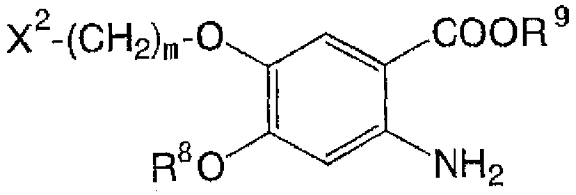
[Claim 13]

Formula (10) :



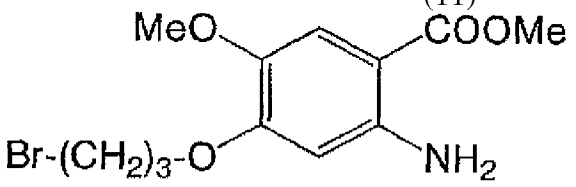
(10)

R8 shows an alkyl group among [type, R9 shows a hydrogen atom or a hydrocarbon group, and X2 shows a halogen atom. m shows the integer of 2-4.] Formula (5) characterized by coming out and returning the 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative shown :



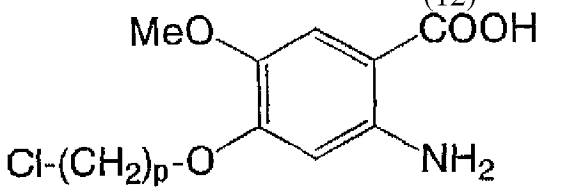
(5)

R8, R9, X2, and m are synonymous with the above among [type.]
The process of the 4-alkoxy 5-halogeno alkoxy anthranilic acid derivative come out of and shown.
[Claim 14]
A process given in the claim 13 which performs the above-mentioned reduction under hydrogen atmosphere or Gyi acid existence under existence of a metal catalyst.
[Claim 15]
A process given in the claim 14 whose metal catalyst is the thing which is chosen from the group which consists of palladium, platinum, and nickel, and which contains one metal atom at least.
[Claim 16]
Formula (11) :



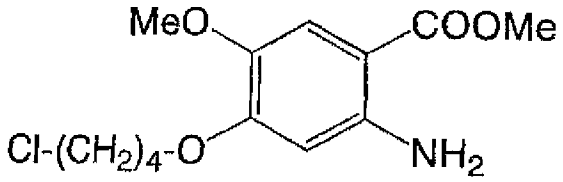
(11)

Me shows a methyl group among [type.]
5-********- 4-(3-bromo propoxy) methyl anthranilate come out of and shown.
[Claim 17]
Formula (12) :



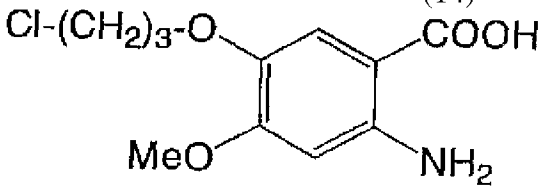
(12)

Me shows a methyl group among [type and p is 2 or 3.]
5-********- 4-chloro alkoxy anthranilic acid come out of and shown.
[Claim 18]
Formula (13) :



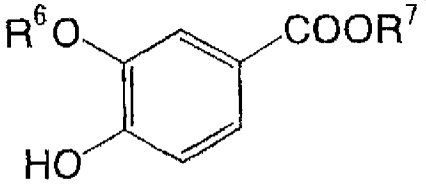
(13)

Me shows a methyl group among [type.] 5-********- 4-(4-chloro butoxy) methyl anthranilate come out of and shown. [Claim 19] Formula (14) :



(14)

Me shows a methyl group among [type.] 4-********- 5-(3-chloro propoxy) anthranilic acid come out of and shown. [Claim 20] Formula (15) :

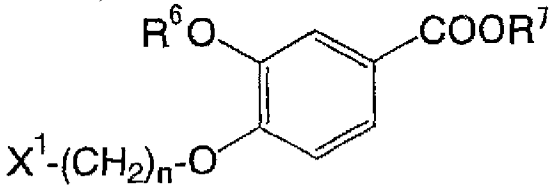


(15)

An alkyl group and R7 show a hydrogen atom or a hydrocarbon group R6 among [type.] The 3-alkoxy 4-hydroxybenzoic acid derivative come out of and shown, and formula (16) :

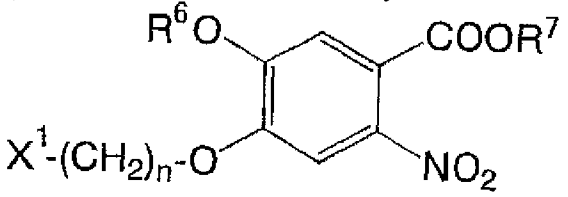
$$X^3-(CH_2)_n-X^4 \qquad (16)$$

X3 and X4 show a halogen atom among [type, and n shows the integer of 2-4. Come out, dihalogeno Alekan shown is made to react under existence of a base and in an organic solvent, and it is a formula (17). :



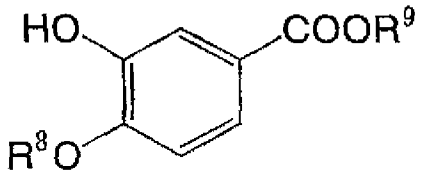
(17)

R6, R7, and n are synonymous with the above among [type, and X1 is a halogen atom corresponding to either X3 or X4.]
the first process out of which it comes and which is used as the 3-alkoxy 4-halogeno alkoxy benzoic acid derivative shown -- and
The second process which make nitric acid react to the above-mentioned 3-alkoxy 4-halogeno alkoxy benzoic acid derivative, and it is made to nitrate under existence of alkaline metal nitrite salt,
Formula (9) characterized by becoming by ****** :



(9)

R6, R7, X1, and n are synonymous with the above among [type.]
The process of the 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative come out of and shown.
[Claim 21]
A process given in the claim 20 whose organic solvents of the first process are nitril, ketone, or those mixed solvents.
[Claim 22]
A process given in the claim 20 whose amount of the base used in the first process is 1.1-2.5mol to 1mol of 3-alkoxy 4-hydroxybenzoic acid derivatives.
[Claim 23]
A process given in the claim 20 which reacts the second process in carboxylic acid.
[Claim 24]
Formula (18) :

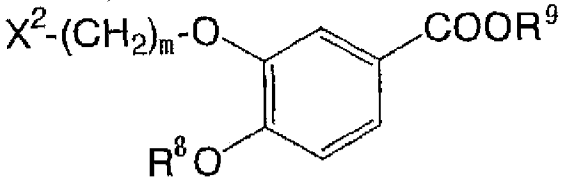


(18)

R8 shows an alkyl group among [type, and R9 shows a hydrogen atom or a hydrocarbon group.]
The 4-alkoxy 3-hydroxybenzoic acid derivative come out of and shown, and formula (19) :

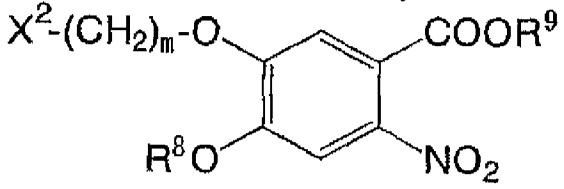
$$X^5-(CH_2)_m-X^6 \qquad (19)$$

X5 and X6 show a halogen atom among [type, and m shows the integer of 2-4.] Come out, dihalogeno Alekan shown is made to react under existence of a base and in an organic solvent, and it is a formula (20). :



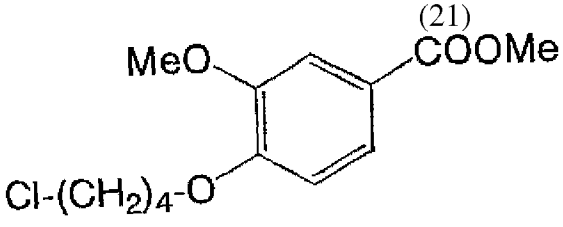
(20)

R8, R9, and m are synonymous with the above among [type, and X2 is a halogen atom corresponding to either X5 or X6. the first process used as the 4-alkoxy 3-halogeno alkoxy benzoic acid derivative shown by] -- and
The second process which make nitric acid react to the above-mentioned 4-alkoxy 3-halogeno alkoxy benzoic acid derivative under existence of alkaline metal nitrite salt, and it is made to nitrate,
Formula (10) characterized by becoming by ****** :



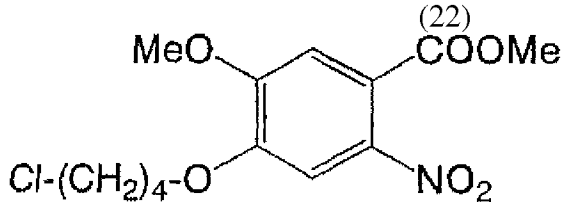
(10)

R8, R9, X2, and m are synonymous with the above among [type.
The process of the 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative come out of and shown.
[Claim 25]
A process given in the claim 24 whose organic solvents of the first process are nitril, ketone, or those mixed solvents.
[Claim 26]
A process given in the claim 24 whose amount of the base used in the first process is 1.1-2.5mol to 1mol of 4-alkoxy 3-hydroxybenzoic acid derivatives.
[Claim 27]
A process given in the claim 24 which reacts the second process in carboxylic acid.
[Claim 28]
Formula (21) :



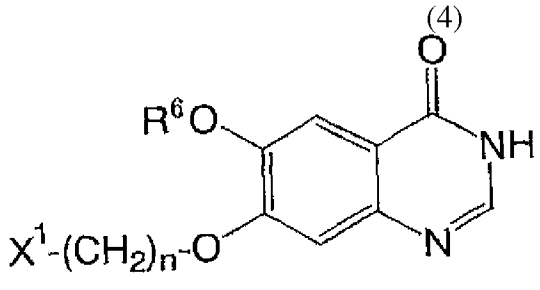
(21)

Me shows a methyl group among [type.]
4-(4-chloro butoxy)-3-METOKISHI methyl benzoate come out of and shown.
[Claim 29]
Formula (22) :



(22)

Me shows a methyl group among [type.]
4-(4-chloro butoxy)-5-********- 2-nitroglycerine methyl benzoate come out of and shown.
[Claim 30]
Formula (4) :

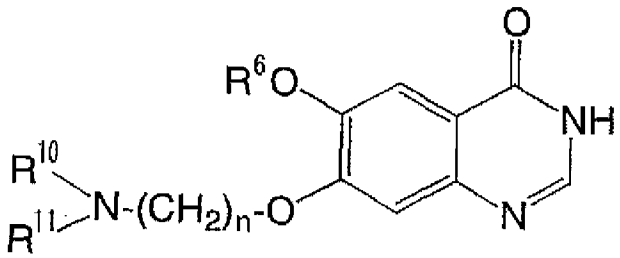


(4)

R6 shows an alkyl group among [type, and X1 shows a halogen atom. n shows the integer of 2-4.]
The 6-alkoxy 7-halogeno alkoxy quinazoline 4-ON and the formula (23) which are come out of and shown :

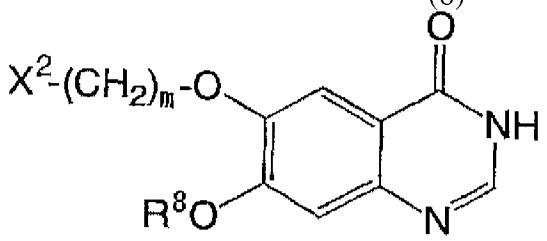
$$R^{10}-NH-R^{11} \qquad (23)$$

R10 and R11 show among [type the hydrocarbon group which may contain the hydrogen atom or the hetero atom. In addition, it may combine with each other and R10 and R11 may form a hydrocarbon ring or heterocycle.]
Formula (24) characterized by coming out and making the amine compound shown react :



(24)

R6, R10, and R11 are synonymous with the above among [type.]
The process of the 6-alkoxy 7-amino alkoxy quinazoline 4-ON derivative come out of and shown.
[Claim 31]
Formula (6) :

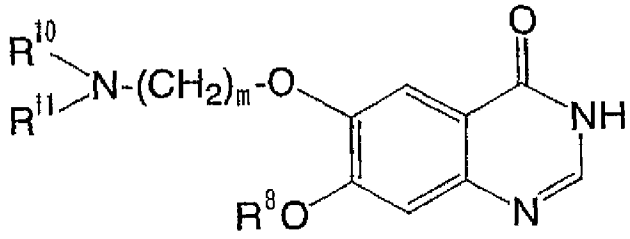


(6)

R8 shows an alkyl group among [type, and X2 shows a halogen atom. m shows the integer of 2-4.]
The 7-alkoxy 6-halogeno alkoxy quinazoline 4-ON and the formula (23) which are come out of and shown :

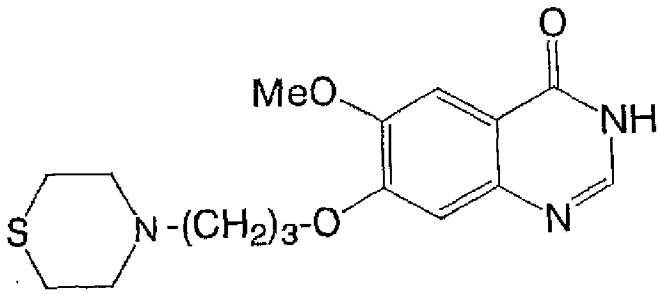
$$R^{10}-NH-R^{11} \qquad (23)$$

R10 and R11 show among [type the hydrocarbon group which may contain the hydrogen atom or the hetero atom. In addition, it may combine with each other and R10 and R11 may form a hydrocarbon ring or heterocycle.]
Formula (25) characterized by coming out and making the amine compound shown react :



(25)

R8, R10, R11, and m are synonymous with the above among [type.]
The process of the 7-alkoxy 6-amino alkoxy quinazoline 4-ON derivative come out of and shown.
[Claim 32]
Formula (26) :



(26)

Me shows a methyl group among [type.]
6-********- 7-(3-thiomorpholino propoxy) quinazoline 4-ON come out of and shown.
[Claim 33]
A process given in the claim 1 R1, R3, and whose R4 are hydrogen atoms and whose R2 is an iodine atom.
[Claim 34]
A process given in the claim 1 R1 and whose R4 are hydrogen atoms and R2 and whose R3 are 2-methoxyethoxy machines.

[Detailed Description of the Invention]
[Field of the Invention]
This invention relates to the method of manufacturing a quinazoline 4-ON derivative from an anthranilic acid derivative. A quinazoline 4-ON derivative is a compound useful as synthetic intermediate or materials, such as medicine and agricultural chemicals. This invention relates to the method of manufacturing a 6-alkoxy 7-amino alkoxy quinazoline 4-ON derivative or a 7-alkoxy 6-amino alkoxy quinazoline 4-ON derivative, from a quinazoline 4-ON derivative again. A 6-alkoxy 7-amino alkoxy quinazoline 4-ON derivative and a 7-alkoxy 6-amino alkoxy quinazoline 4-ON derivative are compounds useful as synthetic intermediate or materials, such as medicine and agricultural chemicals.
This invention relates also to the method of manufacturing an anthranilic acid derivative useful as materials of a new quinazoline 4-ON derivative and its quinazoline 4-ON derivative again.
This invention relates also to the method of manufacturing the above-mentioned anthranilic acid derivative from a nitroglycerine benzoic acid derivative again. This invention is a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or a 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative again. It is related with the method of manufacturing from a 3-alkoxy 4-hydroxybenzoic acid derivative or a 4-alkoxy 3-hydroxybenzoic acid derivative.
[Background of the Invention]
As a method of manufacturing a quinazoline 4-ON derivative from an anthranilic acid derivative, the following method is known conventionally.
The method of making 5-iodine anthranilic acid and acetic acid HORUMU friend gin react to the Europe public presentation patent application No. 1029853 gazette in ethanol for 20 hours, and manufacturing ** and 6-iodine quinazoline 4-ON is indicated.

However, there is a problem that reaction time must use expensive acetic acid HORUMU friend gin superfluously for a long top in this method.
Anthranilic acid and HORUMU amide are made to react to Chem.Pharm.Bull., and 46 and 1926 (1998), and the method of manufacturing quinazoline 4-ON is indicated. However, by this method, there is a problem that the existing teratogenicity HORUMU amide must be used superfluously.
J. Methyl anthranilate and HORUMU amide are made to react to Org.Chem. and 18,138 (1953) under existence of ammonium formate, and the method of manufacturing quinazoline 4-ON is indicated. However, there is a problem of having to make it react at high temperature, using the existing teratogenicity HORUMU amide superfluously in this method upwards, and there is a problem that **** of an object is low in it.
Any above method contained various problems and it was not advantageous as the industrial manufacture method of a quinazoline 4-ON derivative.
WO As how to manufacture a 6-alkoxy 7-amino alkoxy quinazoline 4-ON derivative or a 7-alkoxy 6-amino alkoxy quinazoline 4-ON derivative to 01/21594 For example, HORUMU amide is made to react to 3-********- 4-(3-morpholino propoxy)-6-ethyl aminobenzoate, and the method of manufacturing 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON by 68% of **** is indicated. However, it cannot be said that this method has the problem of **** having to make it react to a low top at high temperature, using the existing teratogenicity HORUMU amide superfluously etc., and is advantageous as an industrial process.
As how to manufacture a 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative in JP,2001-519788,A from a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative For example, to 4-(3-chloro propoxy)-5-********- 2-nitroglycerine methyl benzoate in the mixed solvent of water and methanol Iron and ammoniumchloride of an overlarge are made to act, and the method of manufacturing 2-amino 4-(3-chloro propoxy)-5-METOKISHI methyl benzoate (4-(3-chloro propoxy)-5-METOKI cyanogen truck nil acid MECHIRU) by 90% of **** is indicated.
J. Med.Chem., and 44 and 3965 (2001), As a method of manufacturing a 4-alkoxy 5-halogeno alkoxy anthranilic acid derivative from a 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative For example, to 5-(3-chloro propoxy)-4-********- 2-nitroglycerine methyl benzoate in the mixed solvent of water and methanol Iron and ammoniumchloride of an overlarge are made to act, and the method of manufacturing 2-amino 5-(3-chloro propoxy)-4-METOKISHI methyl benzoate (5-(3-chloro propoxy)-4-METOKI cyanogen truck nil acid MECHIRU) by 93% of **** is indicated.
however, the above-mentioned method -- each -- a large -- in order to have to use superfluous iron, post-processing becomes complicated and it cannot be said that it is advantageous as an industrial process.
WO As how to manufacture a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative from a 3-alkoxy 4-hydroxybenzoic acid derivative in a No. 02/36587 gazette, Under existence of N-butyl ammonium star's picture and in potassium carbonate solution Make ethyl vanillate (4-hydroxy 3-METOKISHI benzoic acid ethyl) and 3-bromo 1-chloro propane react, make with 4-(3-chloro propoxy)-3-METOKISHI benzoic acid ethyl, and subsequently In the mixed solvent of a methylene chloride and acetic acid, nitric acid is made to react to 4-(3-chloro propoxy)-3-METOKISHI benzoic acid ethyl 70%, and the method of obtaining 4-chloro propoxy 3-********- 2-nitroglycerine

benzoic acid ethyl by 82% (ethyl vanillate standard) of sum total **** is indicated. Aforementioned J.Med.Chem., and 44 and 3965 (2001), As a method of manufacturing a 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative from a 4-alkoxy 3-hydroxybenzoic acid derivative Under existence of bird KAPUCHIRU methylanmmonium chloride and in potassium carbonate solution Make 3-hydroxy 4-METOKISHI methyl benzoate and 3-chloropropyl p-toluene sulfonate react, make with 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate, and subsequently Nitric acid is made to react to 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate 70% in the mixed solvent of a methylene chloride and acetic acid. The method of obtaining 5-(3-chloro propoxy)-4-********- 2-nitroglycerine methyl benzoate by 61% (3-hydroxy 4-METOKISHI methyl benzoate standard) of **** is indicated. However, by the above-mentioned method, since the system of reaction is a complicated 2 ** system, reaction operating it turns complicated up, and it is a reaction solvent. an unsuitable methylene chloride must be used industrially and reaction time is a long time -- being also alike -- it does not start and **** of an object cannot say that it is advantageous as an industrial process from low Reasons.

[An indication of invention]

This invention aims at the thing which can manufacture a quinazoline 4-ON derivative by quantity **** from an anthranilic acid derivative and for which the manufacture method of a suitable quinazoline 4-ON derivative is offered industrially by a simple method under a mild condition.

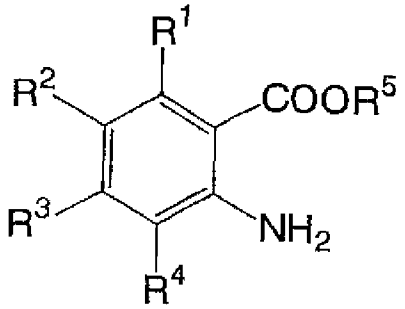
This invention is that of obtaining a 6-alkoxy 7-amino alkoxy quinazoline 4-ON derivative and a 7-alkoxy 6-amino alkoxy quinazoline 4-ON derivative by quantity **** by a simple method under a mild condition again. Also let the thing to cut and for which a suitable process is offered industrially be the purpose.

This invention also makes it the purpose to offer the method that a new quinazoline 4-ON derivative and its quinazoline 4-ON derivative can be industrially manufactured advantageously from a new anthranilic acid derivative again.

This invention also makes it the purpose to offer the method that the above-mentioned new anthranilic acid derivative can be industrially manufactured advantageously from a nitroglycerine benzoic acid derivative again.

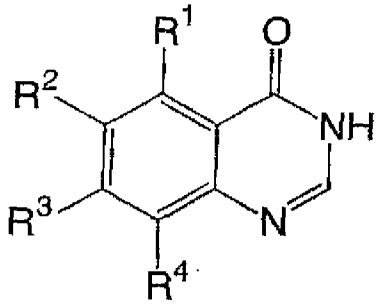
Further this invention [a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or a 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative] With that of manufacturing advantageously industrially from a 3-alkoxy 4-hydroxybenzoic acid derivative or a 4-alkoxy 3-hydroxybenzoic acid derivative Also let it be the purpose to offer the method of cutting.

This invention is a formula (1). :



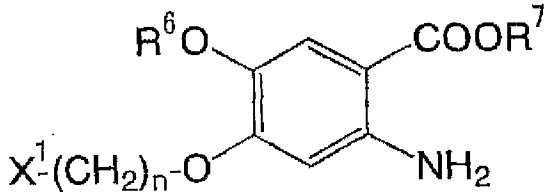
(1)

Among [type, R1, R2, R3, and R4 may be the same or different, respectively, and show the basis which does not participate in the following reaction. In addition, it may combine with each other and R1, R2, R3, and R4 may form the ring. R5 shows a hydrogen atom or a hydrocarbon group.]
Formula (2) characterized by coming out and making the anthranilic acid derivative shown and a Gyi acid derivative react under existence of carboxylic acid ammonium :



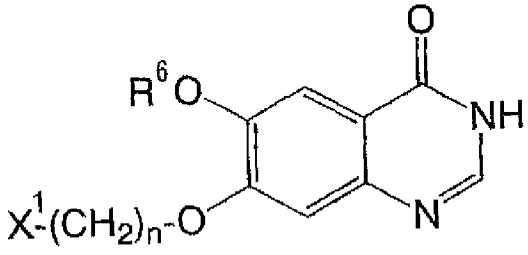
(2)

R1, R2, R3, and R4 are synonymous with the above among [type.]
It comes out and is in the manufacture method of the quinazoline 4-ON derivative shown. This invention is a formula again (3). :



(3)

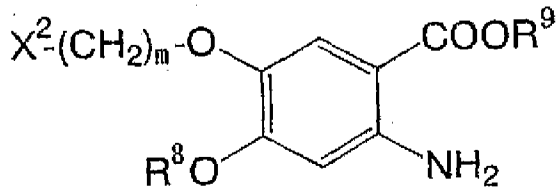
R6 shows an alkyl group among [type, R7 shows a hydrogen atom or a hydrocarbon group, and X1 shows a halogen atom. n shows the integer of 2-4.]
Formula (4) characterized by coming out and making the 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative shown and a Gyi acid derivative react under existence of carboxylic acid ammonium :



(4)

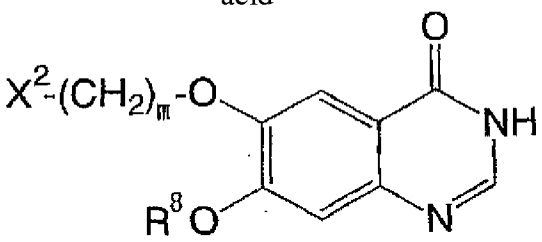
R6, X1, and n are synonymous with the above among [type.]
It comes out and is also in the process of 6-alkoxy 7-halogeno alkoxy quinazoline 4-ON

shown.
This invention is a formula again (5). :



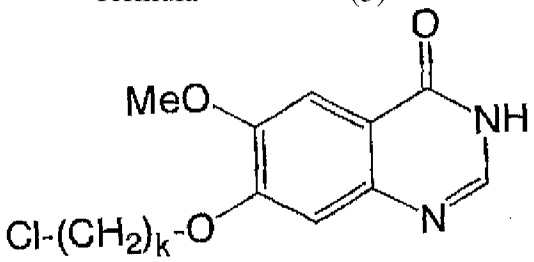
(5)

R8 shows an alkyl group among [type, R9 shows a hydrogen atom or a hydrocarbon group, and X2 shows a halogen atom. m shows the integer of 2-4.]
Formula (6) characterized by coming out and making the 4-alkoxy 5-halogeno alkoxy anthranilic acid derivative shown and a Gyi acid derivative react under existence of carboxylic acid ammonium :



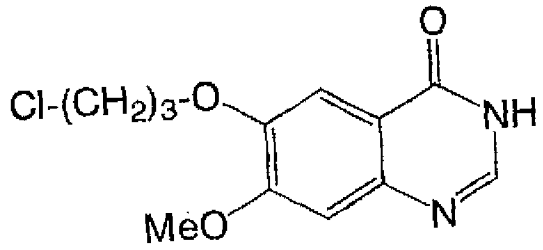
(6)

R8, X2, and m are synonymous with the above among [type.]
It comes out and is also in the process of 7-alkoxy 6-halogeno alkoxy quinazoline 4-ON shown.
This invention is a formula which is the new molecular entity included by the above-mentioned formula (3) again (7). :



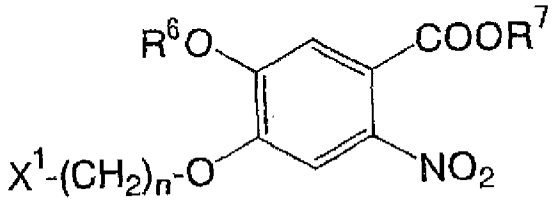
(7)

Me shows a methyl group among [type and k shows the integer of 2-4.]
It comes out and is also in the 6-********- 7-(3-chloro alkoxy) quinazoline 4-ON shown.
This invention is a formula which is the new molecular entity included by the above-mentioned formula (6) again (8). :



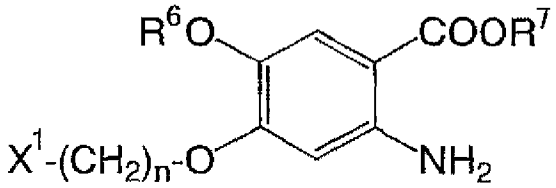
(8)

Me shows a methyl group among [type.]
It comes out and is also in the 7-********- 6-(3-chloro propoxy) quinazoline 4-ON shown.
Furthermore, this invention is a formula (9). :



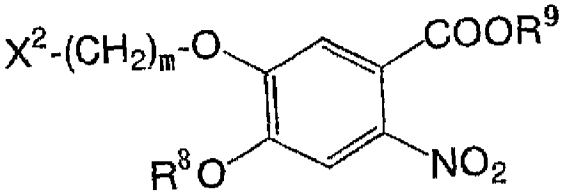
(9)

R6 shows an alkyl group among [type, R7 shows a hydrogen atom or a hydrocarbon group, and X1 shows a halogen atom. n shows the integer of 2-4.]
Formula (3) characterized by coming out and returning the 6-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative shown :



(3)

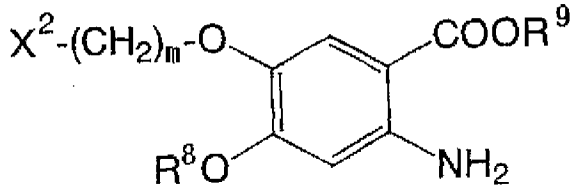
R6, R7, X1, and n are synonymous with the above among [type.]
It comes out and is also in the process of the 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative shown.
Furthermore, this invention is a formula again (10). :



(10)

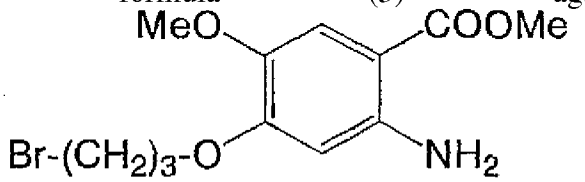
R8 shows an alkyl group among [type, R9 shows a hydrogen atom or a hydrocarbon

group, and X2 shows a halogen atom. m shows the integer of 2-4.]
Formula (5) characterized by coming out and returning the 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative shown :



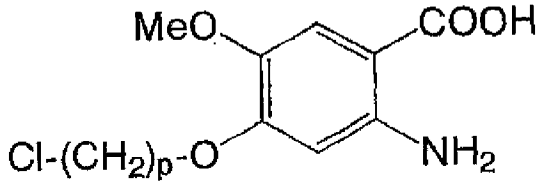
(5)

R8, R9, X2, and m are synonymous with the above among [type.]
It comes out and is also in the process of the 4-alkoxy 5-halogeno alkoxy anthranilic acid derivative shown.
This invention is a formula which is the new molecular entity included by the above-mentioned formula (3) again (11). :



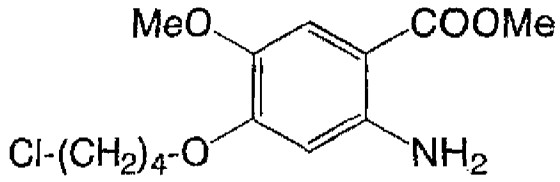
(11)

Me shows a methyl group among [type.]
It comes out and is also in the 5-********- 4-(3-bromo propoxy) methyl anthranilate shown.
This invention is a formula which is the new molecular entity included above (3) again (12). :



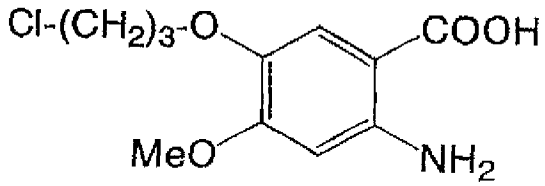
(12)

Me shows a methyl group among [type and p is 2 or 3.]
It comes out and is also in the 5-********- 4-chloro alkoxy anthranilic acid shown.
This invention is a formula which is the new molecular entity included above (3) again (13). :



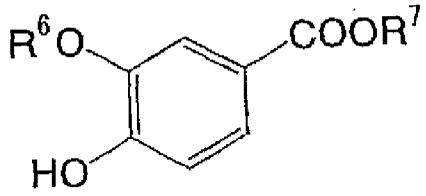
(13)

Me shows a methyl group among [type.]
It comes out and is also in the 5-********- 4-(4-chloro butoxy) methyl anthranilate shown.
This invention is a formula which is the new molecular entity included above (5) again (14). :



(14)

Me shows a methyl group among [type.]
It comes out and is also in the 4-********- 5-(3-chloro propoxy) anthranilic acid shown.
This invention is a formula again (15). :

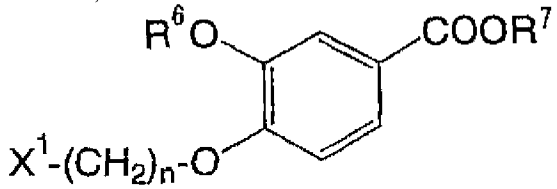


(15)

An alkyl group and R7 show a hydrogen atom or a hydrocarbon group R6 among [type.]
The 3-alkoxy 4-hydroxybenzoic acid derivative come out of and shown, and formula (16) :

$$X^3-(CH_2)_n-X^4 \qquad (16)$$

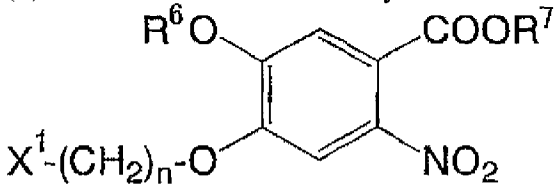
X3 and X4 show a halogen atom among [type, and n shows the integer of 2-4.
Come out, dihalogeno Alekan shown is made to react under existence of a base and in an organic solvent, and it is a formula (17). :



(17)

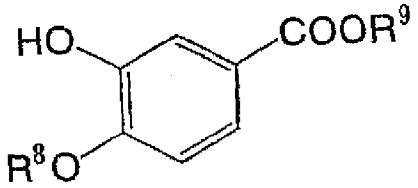
R6, R7, and n are synonymous with the above among [type, and X1 is a halogen atom corresponding to either X3 or X4.]
the first process out of which it comes and which is used as the 3-alkoxy 4-halogeno alkoxy benzoic acid derivative shown -- and

The second process which make nitric acid react to the above-mentioned 3-alkoxy 4-halogeno alkoxy benzoic acid derivative, and it is made to nitrate under existence of alkaline metal nitrite salt, Formula (9) characterized by becoming by ****** :



(9)

R6, R7, X1, and n are synonymous with the above among [type.] It comes out and is also in the process of the 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative shown. This invention is a formula again (18). :

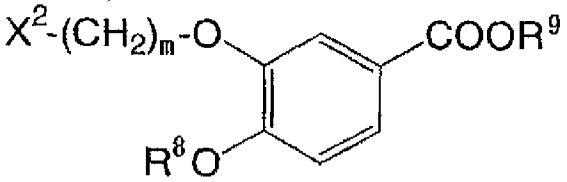


(18)

R8 shows an alkyl group among [type, and R9 shows a hydrogen atom or a hydrocarbon group.]
The 4-alkoxy 3-hydroxybenzoic acid derivative come out of and shown, and formula (19) :

$$X^5-(CH_2)_m-X^6 \qquad (19)$$

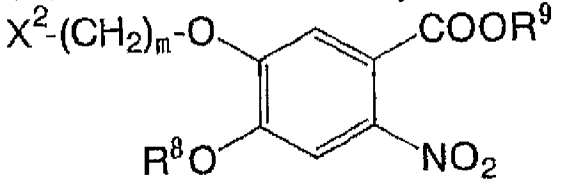
X5 and X6 show a halogen atom among [type, and m shows the integer of 2-4.] Come out, dihalogeno Alekan shown is made to react under existence of a base and in an organic solvent, and it is a formula (20). :



(20)

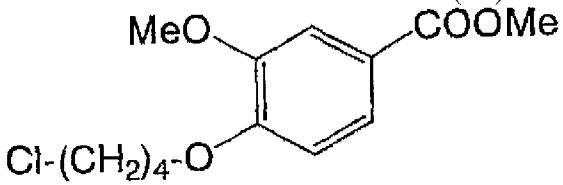
R8, R9, and m are synonymous with the above among [type, and X2 is a halogen atom corresponding to either X5 or X6. the first process used as the 4-alkoxy 3-halogeno alkoxy benzoic acid derivative shown by] -- and
The second process which make nitric acid react to the above-mentioned 4-alkoxy 3-

halogeno alkoxy benzoic acid derivative under existence of alkaline metal nitrite salt, and it is made to nitrate,
Formula (10) characterized by becoming by ****** :



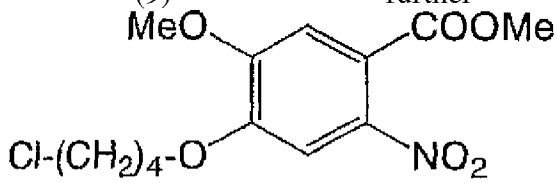
(10)

R8, R9, X2, and m are synonymous with the above among [type.
It comes out and is also in the process of the 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative shown.
This invention is a formula which is the new substance included by the further above-mentioned formula (17) (21). :



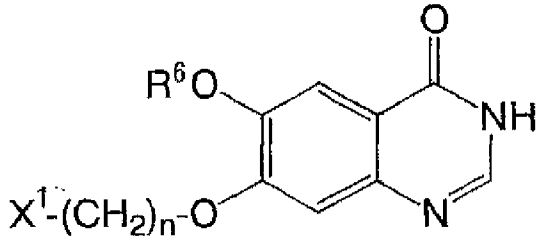
(21)

Me shows a methyl group among [type.]
It comes out and is also in the 4-(4-chloro butoxy)-3-METOKISHI methyl benzoate shown.
This invention is a formula which is the new substance included by the above-mentioned formula (9) further (22). :



(22)

Me shows a methyl group among [type.]
It comes out and is also in the 4-(4-chloro butoxy)-5-********- 2-nitroglycerine methyl benzoate shown.
This invention is a formula further (4). :

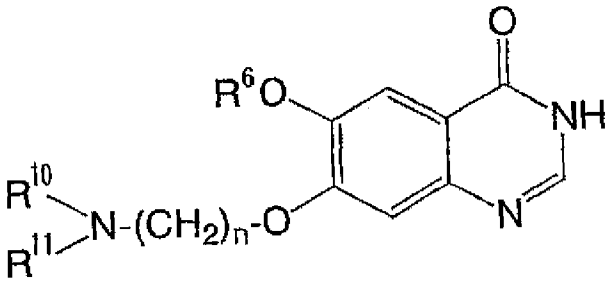


(4)

R6 shows an alkyl group among [type, and X1 shows a halogen atom. n shows the integer of 2-4.]
The 6-alkoxy 7-halogeno alkoxy quinazoline 4-ON and the formula (23) which are come out of and shown :

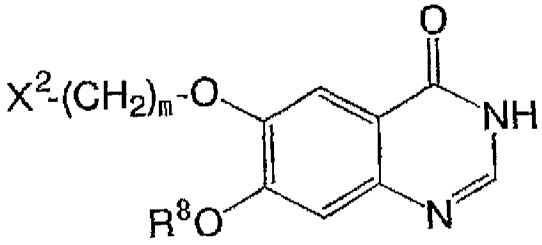
$$R^{10}-NH-R^{11} \qquad (23)$$

R10 and R11 show among [type the hydrocarbon group which may contain the hydrogen atom or the hetero atom. In addition, it may combine with each other and R10 and R11 may form a hydrocarbon ring or heterocycle.]
Formula (24) characterized by coming out and making the amine compound shown react :



(24)

R6, R10, and R11 are synonymous with the above among [type.]
It comes out and is also in the process of the 6-alkoxy 7-amino alkoxy quinazoline 4-ON derivative shown.
This invention is a formula further (6). :

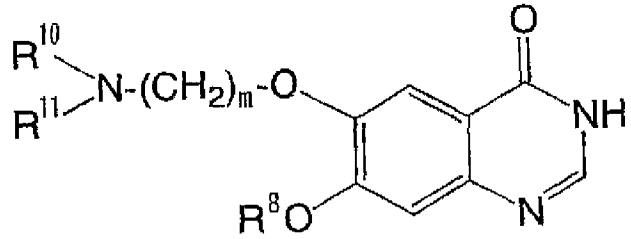


(6)

R8 shows an alkyl group among [type, and X2 shows a halogen atom. m shows the integer of 2-4.]
The 7-alkoxy 6-halogeno alkoxy quinazoline 4-ON and the formula (23) which are come out of and shown :

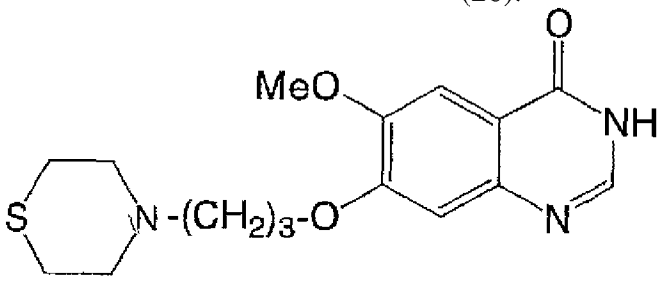
$$R^{10}-NH-R^{11} \qquad (23)$$

R10 and R11 show among [type the hydrocarbon group which may contain the hydrogen atom or the hetero atom. In addition, it may combine with each other and R10 and R11 may form a hydrocarbon ring or heterocycle.]
Formula (25) characterized by coming out and making the amine compound shown react :



(25)

R8, R10, R11, and m are synonymous with the above among [type.]
It comes out and is also in the process of the 7-alkoxy 6-amino alkoxy quinazoline 4-ON derivative shown.
This invention is a formula which is the new substance included by the formula (24) again (26). :



(26)

Me shows a methyl group among [type.]
It comes out and is also in the 6-********- 7-(3-thiomorpholino propoxy) quinazoline 4-ON shown.
Next, this invention is explained in detail.
Although it is the basis which R1, R2, R3, and R4 may be the same or different, and may have a substituent in the anthranilic acid derivative of the general formula (1) used in this invention and which does not participate in a reaction, Specifically, a hydrogen atom, an alkyl group, a cycloalkyl machine, an ARARUKIRU machine, an aryl group, a halogen atom, a hydronalium KISHIRU machine, an alkoxyl group, an ARUKIRUCHIO machine, a nitro group, a cyano group, a carbonyl group, an amino group (except for R1), or a carboxyl group (except for R4) is shown, for example. In addition, it may combine with each other and R1, R2, R3, and R4 may form the ring.
As the above-mentioned alkyl group, an alkyl group with 1-12 carbon atoms, such as a methyl group, an ethyl group, a propyl group, a butyl group, the Penn Chill machine, a hexyl group, a HEPUCHIRU machine, an OKUCHIRU machine, a NONIRU machine, and a decyl group, is mentioned, for example. In addition, these bases include various

opposite-sex objects.
As the above-mentioned cycloalkyl machine, a cycloalkyl machine with 3-12 carbon atoms, such as a cyclo propyl group, a cyclo butyl group, a cyclopentylic group, a cyclohexyl machine, a cycloheptyl machine, and a cyclo OKUCHIRU machine, is mentioned, for example.
As the above-mentioned ARARUKIRU machine, an ARARUKIRU machine with 7-14 carbon atoms, such as a benzyl group, a FENECHIRU machine, and a phenylpropyl machine, is mentioned, for example. In addition, these bases include various opposite-sex objects.
As the above-mentioned aryl group, an aryl group with 6-14 carbon atoms, such as a phenyl group, p-trill machine, the Naff Chill machine, and an anthranil, is mentioned, for example. In addition, these bases include various opposite-sex objects.
As the above-mentioned halogen atom, a fluoride atom, a chlorine atom, a bromine atom, and an iodine atom are mentioned, for example.
As the above-mentioned alkoxyl group, an alkoxyl group with 1-12 carbon atoms, such as a methoxyl group, an ethoxyl group, and propoxyl, is mentioned, for example. In addition, these bases include various opposite-sex objects.
As the above-mentioned ARUKIRUCHIO machine, an alkyl group with 1-12 carbon atoms, such as a MECHIRUCHIO machine, an ECHIRUCHIO machine, and a pro PIRUCHIO machine, is mentioned, for example. In addition, these bases include various opposite-sex objects.
An alkyl group, a cycloalkyl machine, an ARARUKIRU machine, an aryl group, an alkoxyl group, an aforementioned ARUKIRUCHIO machine, or an aforementioned amino group (except for R1) may have a substituent. As the substituent, the substituent through a carbon atom, the substituent through an oxygen atom, the substituent through a nitrogen atom, the substituent through a sulfur atom, a halogen atom, etc. are mentioned.
As a substituent through said carbon atom, they are a methyl group and an ethyl group, for example, Alkyl groups, such as a propyl group, a butyl group, the Penn Chill machine, and a hexyl group; A cyclo propyl group, Cycloalkyl machines, such as a cyclo butyl group, a cyclopentylic group, a cyclohexyl machine, and a cyclo butyl group; A vinyl group, An allyl group, a propenyl machine, a cyclo propenyl machine, a cyclo butenyl group, Alkenyl groups, such as a cyclo pentenyl machine; A pyrrolidyl machine, a pyrrolyl machine, Heterocyclic machines, such as a frill machine and a CHIENIRU machine; A phenyl group, a trill machine, a KISHIRIRU machine, Aryl groups, such as a BIFENIRU machine, the Naff Chill machine, an anthryl machine, and a phenan trill machine; A formyl group, An acetyl group, a pro PIONIRU machine, an acrylyl group, a pivaloyl machine, a cyclohexyl carbonyl group, Acyl group (ASETARU-ized); carboxyl groups, such as a benzoyl group, a naphthoyl machine, and a TORUOIRU machine; A METOKISHI carbonyl group, alkoxy carbonyl group [, such as an ethoxycarbonyl machine,]; -- aryloxy carbonyl group [, such as a FENOKISHI carbonyl group,]; -- alkyl halide machine [, such as a trifluoromethyl machine,]; -- a cyano group is mentioned. In addition, these bases include various opposite-sex objects.
As the substituent through said oxygen atom **, for example, a hydronalium KISHIRU machine,; A methoxyl group, an ethoxyl group, propoxyl, Alkoxyl groups, such as a butoxyl machine, a PENCHIRU oxyl machine, a HEKISHIRU oxyl machine, a HEPUCHIRU oxyl machine, a BENJIRU oxyl machine, a piperidyl oxyl machine, and a

pyranyl oxyl machine; ARIRU oxyl machines, such as a FENOKISHIRU machine, a toluyl oxyl machine, and a NAFUCHIRU oxyl machine, are mentioned. In addition, these bases include various opposite-sex objects.
As the substituent through said nitrogen atom **, for example, a methylamino machine, an ethylamino machine, a butylamino machine, a cyclohexylamino machine, The first amino group, such as a phenylamino machine and the Naff Chill amino group; A dimethylamino machine, A diethylamino machine, a dibutylamino machine, a methylethylamino machine, a methylbutylamino machine, The second amino group, such as a diphenylamino machine; heterocyclic amino group; imino groups, such as a morpholino group, a thiomorpholino machine, a piperidino machine, a piperazinyl machine, a PIRAZORIJINIRU machine, a pyrrolidino machine, and the India Lil machine, are mentioned. In addition, these bases include various opposite-sex objects.
As a substituent through said sulfur atom, CHIOA reel oxyl machines, such as CHIOARUKOKISHIRU machine; CHIOFENOKISHIRU machines, such as a mercapto group; CHIOMETOKISHIRU machine, a CHIOETOKISHIRU machine, and a CHIOPUROPOKISHIRU machine, a CHIOTORUIRU oxyl machine, and a CHIONAFUCHIRU oxyl machine, etc. are mentioned, for example. In addition, these bases include various opposite-sex objects.
As said halogen atom, a fluoride atom, a chlorine atom, a bromine atom, and an iodine atom are mentioned.
Although R5 is a hydrogen atom or a hydrocarbon group, As a hydrocarbon group, for example A methyl group, an ethyl group, a propyl group, a butyl group, Alkyl groups, such as the Penn Chill machine and a hexyl group; A cyclo propyl group, a cyclo butyl group, ARARUKIRU machines, such as cycloalkyl machine; benzyl groups, such as a cyclopentylic group and a cyclohexyl machine, a FENECHIRU machine, and a phenylpropyl machine; aryl groups, such as a phenyl group, a trill machine, the Naff Chill machine, and an anthryl machine, are mentioned. In addition, these bases include various opposite-sex objects.
As the Gyi acid derivative which uses the compound of a formula (1) in the reaction changed into a formula (2), For example, Gyi acid ester, such as Gyi acid; methyl formate and ethyl formate; although ORUTOGI acid ester, such as ORUTOGI acid MECHIRU and ethyl orthoformate, is mentioned desirable -- Gyi acid ester and ORUTOGI acid ester -- further -- desirable -- ORUTOGI acid ester -- ORUTOGI acid MECHIRU and ethyl orthoformate are used especially preferably.
1.0-30mol of the amount of the Gyi acid derivative used is 1.1-10mol still more preferably preferably to 1mol of anthranilic acid derivatives.
As the carboxylic acid ammonium used in the above-mentioned reaction, For example, aliphatic-carboxylic-acid ammonium, such as ammonium formate, ammonium acetate, and propionic acid ammonium; although aromatic-carboxylic-acid ammonium, such as benzoic acid and dichloro benzoic acid, is mentioned desirable -- aliphatic-carboxylic-acid ammonium -- further -- desirable -- ammonium formate and ammonium acetate -- it is ammonium acetate especially preferably. In addition, independent or two sorts or more may be mixed and used for these carboxylic acid ammonium.
1.0-10.0mol of the amount of said carboxylic acid ammonium used is 1.1-6.0mol still more preferably preferably to 1mol of anthranilic acid derivatives.
The above-mentioned reaction is performed under existence of a solvent or nonexistence.

As a solvent to be used, especially if a reaction is not checked, it will not be limited. For example, methanol, ethanol, isopropyl alcohol, n-butyl alcohol, Alcohols;N, such as t-butyl alcohol, N-JIMECHIRUHORUMU amide, Sulfo KISHIDO, such as urea; dimethyl sulfoxide, such as amide;N, such as N-MECHIRU pylori boss, and N'-JIMECHIRU imidazolidinone; Benzene, Aromatic hydrocarbon, such as toluene, xylene, and MESHICHIREN; Chlorination methylene, Although ether, such as nitril; diethylether, such as; acetonitrile, such as halogenated aliphatic hydrocarbon, such as chloroform and dichloro ethane, and a PUROPI demon trill, a tetrahydro franc, and JIOKISAN, is mentioned, desirable -- alcohols, amide, and nitril -- methanol, ethanol, N, and N'-JIMECHIRU imidazolidinone and acetonitrile are used still more preferably. These solvents are independent, or two or more sorts may be mixed and used for them. Although the amount of the solvent used is suitably adjusted by the homogeneity of reaction liquid, churning nature, etc., it is 0-5g especially preferably 0-20g still more preferably 0-50g preferably to 1g of anthranilic acid derivatives.
The above-mentioned reaction is performed by the method of making carboxylic acid ammonium, an anthranilic acid derivative, a Gyi acid derivative, and a solvent mix and agitate in the atmosphere of inactive gas etc., for example. 40-200 degrees C of reaction temperature in that case is 50-150 degrees C still more preferably preferably, and reaction pressure in particular is not restricted.
The quinazoline 4-ON derivative of output is isolated and refined by the general method of depending on filtration after the end of a reaction (for example, extraction), concentration, distillation, a re-crystal, a column chromatography, etc.
Set the compound of the formula (3) of this invention, or a formula (5) for the reaction changed into the compound of a formula (4) or a formula (6), respectively. In the 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative or 4-alkoxy 5-halogeno alkoxy anthranilic acid derivative to be used R6 and R8 are alkyl groups, for example, a methyl group, an ethyl group, a propyl group, a butyl group, the Penn Chill machine, and an alkyl group with 1-12 carbon atoms of hexyl group ****** are mentioned. In addition, these bases include various opposite-sex objects.
R7 and R9 are a hydrogen atom or a hydrocarbon group. As a hydrocarbon group, for example A methyl group, an ethyl group, a propyl group, a butyl group, An alkyl group with 1-12 carbon atoms, such as the Penn Chill machine and a hexyl group; A cyclo propyl group, A cycloalkyl machine with 3-12 carbon atoms, such as a cyclo butyl group, a cyclopentylic group, and a cyclohexyl machine; A benzyl group, An ARARUKIRU machine with 7-14 carbon atoms, such as a FENECHIRU machine and a phenylpropyl machine; an aryl group with 6-14 carbon atoms, such as a phenyl group, a trill machine, the Naff Chill machine, and an anthryl machine, is mentioned. In addition, these bases include various opposite-sex objects.
X1 and X2 are halogen atoms, for example, a fluoride atom, a chlorine atom, a bromine atom, and an iodine atom are mentioned.
n and m show the integer of 2-4, respectively.
Although ORUTOGI acid ester, such as Gyi acid ester; ORUTOGI acid MECHIRU, such as Gyi acid; methyl formate and ethyl formate, and ethyl orthoformate, is mentioned as a Gyi acid derivative used in the above-mentioned reaction, for example, desirable -- Gyi acid ester and ORUTOGI acid ester -- further -- desirable -- ORUTOGI acid ester -- ORUTOGI acid MECHIRU and ethyl orthoformate are used especially preferably.

1.0-30mol of the amount of the Gyi acid derivative used is 1.1-10mol still more preferably preferably to a 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative or 1mol of 4-alkoxy 5-halogeno alkoxy anthranilic acid derivatives.
As the carboxylic acid ammonium used in the above-mentioned reaction, For example, aliphatic-carboxylic-acid ammonium, such as ammonium formate, ammonium acetate, and propionic acid ammonium; although aromatic-carboxylic-acid ammonium, such as ammonium benzoate and dichloro ammonium benzoate, is mentioned desirable -- aliphatic-carboxylic-acid ammonium -- further -- desirable -- ammonium formate and ammonium acetate -- ammonium acetate is used especially preferably. In addition, independent or two sorts or more may be mixed and used for these carboxylic acid ammonium.
1.0-10.0mol of the amount of the carboxylic acid ammonium used is 1.1-6.0mol still more preferably preferably to 1mol of 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative 4-alkoxy 5-halogeno alkoxy anthranilic acid derivatives.
The above-mentioned reaction is performed under existence of a solvent or nonexistence. As a solvent to be used, especially if a reaction is not checked, it will not be limited. For example, methanol, ethanol, isopropyl alcohol, n-butyl alcohol, Alcohols;N, such as t-butyl alcohol, N-JIMECHIRUHORUMU amide, Sulfo KISHIDO, such as urea; dimethyl sulfoxide, such as amide;N, such as N-MECHIRU pylori boss, and N'-JIMECHIRU imidazolidinone; Benzene, Aromatic hydrocarbon, such as toluene, xylene, and MESHICHIREN; Chlorination methylene, Nitril [, such as; acetonitrile and a PUROPI demon trill,], such as halogenated aliphatic hydrocarbon, such as chloroform and dichloro ethane; although ether, such as diethylether, a tetrahydro franc, and JIOKISAN, is mentioned desirable -- alcohols, amide, and nitril -- methanol, ethanol, N, and N'-JIMECHIRU imidazolidinone and acetonitrile are used still more preferably. Independent or two sorts or more may be mixed and used for these solvents.
Although the amount of the solvent used is suitably adjusted by the homogeneity of reaction liquid, churning nature, etc., 0-20g 0-50g is 0-5g especially preferably still more preferably preferably to a 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative or 1g of 4-alkoxy 5-halogeno alkoxy anthranilic acid derivatives.
The above-mentioned reaction is the method of making a 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative or a 4-alkoxy 5-halogeno alkoxy anthranilic acid derivative, a Gyi acid derivative, carboxylic acid ammonium, and a solvent mix and agitate in inactive gas atmosphere etc., for example. It is carried out. 40-200 degrees C of reaction temperature in that case is 50-150 degrees C still more preferably preferably, and reaction pressure in particular is not restricted.
In addition, 6-alkoxy 7-halogeno alkoxy quinazoline 4-ON of output or 7-alkoxy 6-halogeno alkoxy quinazoline 4-ON is after the end of a reaction. For example, it is isolated and refined by general methods, such as filtration, concentration, distillation, a re-crystal, ****, and a column chromatography.
From the compound of the formula (9) of this invention, or a formula (10),, respectively In the 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative which uses the compound of a formula (3) or a formula (5) in the reaction carried out to conversion, R6 and R8 are alkyl groups. For example, an alkyl group with 1-12 carbon atoms is mentioned for a methyl group, an ethyl group, a propyl group, a butyl group, the Penn Chill machine, a

hexyl group, etc. In addition, these bases include various opposite-sex objects.
R7 and R9 are a hydrogen atom or a hydrocarbon group. As a hydrocarbon group, for example A methyl group, an ethyl group, a propyl group, a butyl group, An alkyl group with 1-12 carbon atoms, such as the Penn Chill machine and a hexyl group; A cyclo propyl group, A cycloalkyl machine with 3-12 carbon atoms, such as a cyclo butyl group, a cyclopentylic group, and a cyclohexyl machine; A benzyl group, An ARARUKIRU machine with 7-14 carbon atoms, such as a FENECHIRU machine and a phenylpropyl machine; an aryl group with 6-14 carbon atoms, such as a phenyl group, a trill machine, the Naff Chill machine, and an anthryl machine, is mentioned. In addition, these bases include various opposite-sex objects.
X1 and X2 are halogen atoms, for example, a fluoride atom, a chlorine atom, a bromine atom, and an iodine atom are mentioned.
n and m show the integer of 2-4, respectively.
Especially if the above-mentioned reduction reaction is the method of returning the nitro group directly combined with aromatic compounds to an amino group, it will not be limited, but it is desirable to carry out under existence of a metal catalyst, in hydrogen atmosphere, or under Gyi acid existence.
One metal atom is included at least and it is [which is chosen from the group which consists of palladium, platinum, and nickel as said metal atom] in a concrete target, For example, although palladium/carbon, palladium/barium sulfate, water oxidization palladium / carbon, platinum/carbon, sulfuration platinum / carbon, palladium platinum / carbon, platinum oxide, Raney nickel, etc. are mentioned, palladium/carbon, sulfuration platinum / carbon, and Raney nickel are used preferably. In addition, independent or two sorts or more may be mixed and used for these metal catalysts.
The amount of the above-mentioned metal catalyst used is metal atom conversion, and receives a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or 1g of 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivatives, 0.1-1000mg is 5-500mg still more preferably preferably.
3-50mol of the amount of the above-mentioned hydrogen used is 3-10mol still more preferably preferably to a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or 1mol of 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivatives.
1-100g of the amount of the above-mentioned Gyi acid used is 5-50g still more preferably preferably to a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or 1g of 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivatives.
As the solvent which it is desirable to perform the above-mentioned reaction in existence of a solvent, and it uses, Especially if a reaction is not checked, will not be limited, but For example, water; methanol, Alcohols, such as ethanol, isopropyl alcohol, n-butyl alcohol, and t-butyl alcohol; Acetic acid MECHIRU, Aromatic hydrocarbon, such as carboxylate ester; benzene, such as ethyl acetate and methyl propionate, toluene, xylene, and MESHICHIREN; although ether, such as diethylether, a tetrahydro franc, and JIOKISAN, is mentioned desirable -- alcohols and carboxylate ester -- methanol, ethanol, and ethyl acetate are used still more preferably. In addition, independent or two sorts or more may be mixed and used for these solvents.
Although the amount of the solvent used is suitably adjusted by the homogeneity of reaction liquid, churning nature, etc., 1-100g is 3-30g still more preferably preferably to a

5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or 1g of 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivatives.
The above-mentioned reaction, for example under existence of hydrogen gas or existence of Gyi acid (you may dilute with inactive gas) The method of making a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or a 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative, a metal catalyst, and a solvent mix and agitate etc. It is carried out. 0-300 degrees C of reaction temperature in that case is 20-200 degrees C still more preferably preferably, and reaction pressure is 0.1 - 2MPa still more preferably 0.1 to 10 MPa preferably.
although acid and activated carbon may be added and organic acid, such as inorganic acid; Gyi acid, such as chloride, nitric acid, sulfuric acid, and phosphorus acid, acetic acid, and propionic acid, is mentioned as acid at the above-mentioned reduction reaction, for example, in order to raise reactivity -- desirable -- organic acid -- acetic acid is used still more preferably. In addition, even if independent or two sorts or more may be mixed and used for these acid and acid and activated carbon are simultaneously used for it, it is not cared about.
0.01-20mol of the amount of the above-mentioned acid used is 0.1-5.0mol still more preferably preferably to a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or 1mol of 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivatives.
0.01-10g of the amount of the above-mentioned activated carbon used is 0.1-5.0g still more preferably preferably to a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or 1g of 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivatives.
The 5-alkoxy 4-halogeno alkoxy anthranilic acid derivative of output or a 4-alkoxy 5-halogeno alkoxy anthranilic acid derivative is isolated and refined after the end of a reaction by general methods, such as filtration, concentration, distillation, a re-crystal, ****, and a column chromatography.
Next, how to manufacture the formula (9) of this invention or the compound of (10) from the compound of a formula (15) or a formula (18) is explained.
This method consists of the first process which changes the compound of a formula (15) or a formula (18) into the compound of a formula (17) or a formula (20), and the second process which changes the compound of a formula (17) or a formula (20) into a formula (9) or the compound of (10).
Next, these two processes are explained one by one.
(A) The first process
The first process is the bottom of existence of a base, a 3-alkoxy 4-hydroxybenzoic acid derivative, or a 4-alkoxy 3-hydroxybenzoic acid derivative, It is the process which dihalogeno Alekan is made to react in an organic solvent, and uses him as a 3-alkoxy 4-halogeno alkoxy benzoic acid derivative or a 4-alkoxy 3-halogeno alkoxy benzoic acid derivative.
The 3-alkoxy 4-hydroxybenzoic acid derivative or 4-alkoxy 3-hydroxybenzoic acid derivative used at the first process is shown by an aforementioned general formula (15) or an aforementioned formula (18). In a formula (15) and (18), R6 and R8 are alkyl groups, for example, an alkyl group with 1-12 carbon atoms, such as a methyl group, an ethyl group, a propyl group, a butyl group, the Penn Chill machine, and a hexyl group, is mentioned. In addition, these bases include various opposite-sex objects.

R7 and R9 are a hydrogen atom or a hydrocarbon group. As a hydrocarbon group, for example A methyl group, an ethyl group, a propyl group, a butyl group, An alkyl group with 1-12 carbon atoms, such as the Penn Chill machine and a hexyl group; A cyclo propyl group, A cycloalkyl machine with 3-12 carbon atoms, such as a cyclo butyl group, a cyclopentylic group, and a cyclohexyl machine; A benzyl group, An ARARUKIRU machine with 7-14 carbon atoms, such as a FENECHIRU machine and a phenylpropyl machine; an aryl group with 6-14 carbon atoms, such as a phenyl group, a trill machine, the Naff Chill machine, and an anthryl machine, is mentioned. In addition, these bases include various opposite-sex objects.
At the first above-mentioned process, dihalogeno Alekan of said formula (16) or a formula (19) is used. In a formula (16) or a formula (19), X3, X4, and X5 and X6 are halogen atoms, for example, they are a fluoride atom, a chlorine atom, a bromine atom, and an iodine atom.
n and m show the integer of 2-4, respectively.
1.0-100mol of the amount [1.1-50mol of] of the dihalogeno Alekan used is 1.1-15mol especially preferably still more preferably preferably to a 3-alkoxy 4-hydroxybenzoic acid derivative or 1mol of 4-alkoxy 3-hydroxybenzoic acid derivatives.
As a base used in the first process, it is sodium hydroxide, for example, Alkaline metal hydroxide, such as water oxidization potassium; although alkaline metal ARUKOKISHIDO, such as alkaline metal carbonated water matter salt; sodium methoxide, such as alkaline metal carbonate; sodium bicarbonate, such as sodium carbonate and potassium carbonate, and potassium bicarbonate, and potassium METOKISHIDO, is mentioned desirable -- alkaline metal hydroxide and alkaline metal carbonate -- further -- desirable -- alkaline metal carbonate -- potassium carbonate is used especially preferably. In addition, these bases may mix and use independent or two sorts or more.
1.0-2.9mol of the amount [1.1-2.5mol of] of the base used is 1.1-2.0mol especially preferably still more preferably preferably to a 3-alkoxy 4-hydroxybenzoic acid derivative or 1mol of 4-alkoxy 3-hydroxybenzoic acid derivatives.
As an organic solvent used at the first process, especially if a reaction is not checked, it will not be limited. For example, alcohols, such as methanol, ethanol, isopropyl alcohol, and t-butyl alcohol; Acetone, Ketone;N, such as methyl ethyl ketone and methyl isobutyl ketone, N-JIMECHIRUHORUMU amide, Sulfo KISHIDO, such as urea; dimethyl sulfoxide, such as amide;N, such as N-MECHIRU pylori boss, and N'-JIMECHIRU imidazolidinone; Acetonitrile, Nitril, such as a PUROPI demon trill; although aromatic hydrocarbon, such as ether; toluene, such as diethylether, JIISO pro pill ether, a tetrahydro franc, and JIOKISAN, and xylene, is mentioned, ketone and nitril are used preferably. In addition, independent or two sorts or more may be mixed and used for these organic solvents.
Although the amount of the above-mentioned organic solvent used is suitably adjusted by the homogeneity of reaction liquid, or churning nature, it is 5-50g still more preferably 1-100g preferably to a 3-alkoxy 4-hydroxybenzoic acid derivative or 1g of 4-alkoxy 3-hydroxybenzoic acid derivatives.
The first process is performed, for example among inactive gas atmosphere by the method of making a 3-alkoxy 4-hydroxybenzoic acid derivative or a 4-alkoxy 3-hydroxybenzoic acid derivative, dihalogeno Alekan, a base, and an organic solvent mix

and agitate etc. 20-200 degrees C of reaction temperature in that case is 40-120 degrees C still more preferably preferably, and reaction pressure in particular is not restricted. Moreover, in the first process, they are metal chlorides (preferably), such as sodium chloride, potassium chloride, and a calcium chloride, in the system of reaction. By making an alkaline metal chloride or an alkaline-earth-metals chloride exist, generation of suboutput (for example, dimer of output like 1 and 3-bis(2-********- 4-METOKISHIKARUBONIRUFENOKISHI) propane) can be controlled. Independent or two sorts or more may be mixed and used for these metal chlorides. 0.1-20mol of the amount of the metal chloride used is 0.5-10mol still more preferably preferably to a 3-alkoxy 4-hydroxybenzoic acid derivative or 1mol of 4-alkoxy 3-hydroxybenzoic acid derivatives.
Although a 3-alkoxy 4-halogeno alkoxy benzoic acid derivative or a 4-alkoxy 3-halogeno alkoxy benzoic acid derivative is obtained by the first process, For example after the end of a reaction, by the general method of depending on filtration, concentration, distillation, a re-crystal, ****, a column chromatography, etc., once isolating and refining this, it may be used for the second process, but even if it uses it for the second process as it is, without performing isolation and refining, it is not cared about.
In the first process, the 4-alkoxy 3-halogeno alkoxy benzoic acid derivative expressed with the 3-alkoxy 4-halogeno alkoxy benzoic acid derivative or formula (20) expressed with a formula (17) is obtained. In a formula (17) and (20), R6, R7, R8, R9, n, and m are synonymous with the above, X1 shows either X3 or X4, and X2 shows either X5 or X6.
(B) The second process
The second process is nitric acid to the bottom of existence of alkaline metal nitrite salt, a 3-alkoxy 4-halogeno alkoxy benzoic acid derivative, or a 4-alkoxy 3-halogeno alkoxy benzoic acid derivative. It is the process which is made to react, is made to nitrate and is used as a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or a 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative.
1.0-50mol of quantity of the nitric acid used in this second process is 3.0-10mol still more preferably preferably to a 3-alkoxy 4-halogeno alkoxy benzoic acid derivative or 1mol of 4-alkoxy 3-halogeno alkoxy benzoic acid derivatives. in addition, the concentration of nitric acid -- desirable -- 40 to 80 mass % -- it is 50 to 70 mass % still more preferably.
Although sodium nitrite and nitrous acid potassium are mentioned as alkaline metal nitrite salt used in the second process, for example, sodium nitrite is used preferably. 0.001-1mol of the amount of the above-mentioned alkaline metal nitrite salt used is 0.01-0.5mol still more preferably preferably to a 3-alkoxy 4-halogeno alkoxy benzoic acid derivative or 1mol of 4-alkoxy 3-halogeno alkoxy benzoic acid derivatives.
Although it is desirable to carry out under existence of a solvent as for the second process, it will not be limited as a solvent to be used especially if a reaction is not checked, for example, carboxylic acid, such as Gyi acid, acetic acid, propionic acid, and butanoic acid, is mentioned, acetic acid is used preferably. In addition, independent or two sorts or more may be mixed and used for these solvents.
Although the amount of the solvent used is suitably adjusted by the homogeneity of reaction liquid, or churning nature, it is 1.1-20g still more preferably 1-50g preferably to a 3-alkoxy 4-halogeno alkoxy benzoic acid derivative or 1g of 4-alkoxy 3-halogeno alkoxy benzoic acid derivatives.

Although a 5-alkoxy 4-halogeno alkoxy 2-nitroglycerine benzoic acid derivative or a 4-alkoxy 5-halogeno alkoxy 2-nitroglycerine benzoic acid derivative is obtained by the second process, This is isolated and refined, for example after the end of a reaction by the general method of depending on filtration, concentration, distillation, a re-crystal, ****, a column chromatography, etc.
6-alkoxy 7-halogeno alkoxy quinazoline 4-ON of the aforementioned formula (4), and 7-alkoxy 6-halogeno alkoxy quinazoline 4-ON of a formula (6), respectively The method of the following [derivative / of a formula (25) / the 6-alkoxy 7-amino alkoxy quinazoline 4-ON derivative of a formula (24), and / 7-alkoxy 6-amino alkoxy quinazoline 4-ON] It is easily convertible. In each formula, although R6 is an alkyl group, an alkyl group with 1-12 carbon atoms, such as a methyl group, an ethyl group, a propyl group, a butyl group, the Penn Chill machine, and HEKISHIRU, is mentioned, for example. These bases include various opposite-sex objects.
X1 and X2 are halogen atoms, for example, a fluoride atom, a chlorine atom, a bromine atom, and an iodine atom are mentioned.
n and m show the integer of 2-4, respectively.
Although an amine compound is used in the above-mentioned reaction, this amine compound is shown by the aforementioned formula (23). In a formula (23), R10 and R11 are a hydrogen atom or a hydrocarbon group (the hetero atom may be included). For example, a methyl group, an ethyl group, a propyl group, a butyl group, the Penn Chill machine, An alkyl group with 1-12 carbon atoms, such as a hexyl group; A cyclo propyl group, A cycloalkyl machine with 3-12 carbon atoms, such as a cyclo butyl group, a cyclopentylic group, and a cyclohexyl machine; A benzyl group, An ARARUKIRU machine with 7-14 carbon atoms, such as a FENECHIRU machine and a phenylpropyl machine; an aryl group with 6-14 carbon atoms, such as a phenyl group, a trill machine, the Naff Chill machine, and an anthryl machine, is mentioned. In addition, these bases include various opposite-sex objects. As the basis in which may form the ring (heterocycle is also included) in and a ring (heterocycle is also included) is made to combine R10 and R11 mutually, and to form unitedly, For example, a pentamethylene machine, 1-MECHIRU pentamethylene machine, 3-MECHIRU pentamethylene machine, 3-OKISHI pentamethylene machine, 3-CHIOPENTA methylene machine, etc. are mentioned.
1.0-100mol of the amount of said amine compound used is 1.1-10mol still more preferably preferably to 6-alkoxy 7-halogeno alkoxy quinazoline 4-ON or 1mol of 7-alkoxy 6-halogeno alkoxy quinazoline 4-ON.
The above-mentioned reaction is performed under existence of a solvent or nonexistence. As a solvent to be used, especially if a reaction is not checked, it will not be limited. For example, water, methanol, ethanol, isopropyl alcohol, Alcohols;N, such as n-butyl alcohol, sec-butyl alcohol, and t-butyl alcohol, N-JIMECHIRUHORUMU amide, Sulfo KISHIDO, such as urea; dimethyl sulfoxide, such as amide;N, such as N-MECHIRU pylori boss, and N'-JIMECHIRU imidazolidinone; Benzene, Aromatic hydrocarbon, such as toluene, xylene, and MESHICHIREN; Chlorination methylene, Halogenated aliphatic hydrocarbon, such as chloroform and dichloro ethane; Acetonitrile, Nitril, such as a PUROPI demon trill; although ketone, such as ether, such as diethylether, a tetrahydro franc, and JIOKISAN, acetone, methyl ethyl ketone, and diethyl ketone, is mentioned desirable -- water and alcohols -- water, methanol, ethanol, and sec-butyl alcohol are used

still more preferably. In addition, these solvents are independent, or two or more sorts may be mixed and used for them.
Although the amount of the solvent used is suitably adjusted by the homogeneity of reaction liquid, churning nature, etc., 0-50g is 0-20g still more preferably preferably to 6-alkoxy 7-halogeno alkoxy quinazoline 4-ON or the 7-alkoxy 6-halogeno alkoxy quinazoline 4-ON 1g.
The above-mentioned reaction is performed under existence of a base or nonexistence. As a base to be used, they are lithium hydroxide and sodium hydroxide, for example, Alkaline metal hydroxide, such as water oxidization potassium; Lithium carbonate, sodium carbonate, Alkaline metal carbonate, such as potassium carbonate; Carbonated water matter lithium, sodium bicarbonate, Alkaline metal carbonated water matter salt, such as potassium bicarbonate; Sodium phosphate, Alkaline metal orthophosphates, such as potassium phosphate; Acetic acid sodium, potassium acetate, Alkaline metal carboxylate salt, such as sodium propionate and propionic acid potassium; Sodium methoxide, Potassium METOKISHIDO, sodium ethoxide, potassium ETOKISHIDO, Alkaline metal ARUKOKISHIDO, such as potassium t-butoxide; Trimethylamine, The third class amine, such as triethyl amine, ethyl diisopropylamine, JIECHIRU iso propylamine, triisopropyl amine, benzoRUJIMECHIRU amine, and BENJIRUJI ethyl amine; although PIRIJIN, such as PIRIJIN, CHIRUPI lysine, and JIMECHIRUPI lysine, is mentioned desirable -- alkaline metal hydroxide and alkaline metal carbonate -- sodium hydroxide, water oxidization potassium, sodium carbonate, and potassium carbonate are used still more preferably. These bases may mix and use independent or two sorts or more.
0-20mol of the amount of the base used is 0-10mol still more preferably preferably to 6-alkoxy 7-halogeno alkoxy quinazoline 4-ON or 1mol of 7-alkoxy 6-halogeno alkoxy quinazoline 4-ON.
The above-mentioned reaction is performed by the method of making 6-alkoxy 7-halogeno alkoxy quinazoline 4-ON or 7-alkoxy 6-halogeno alkoxy quinazoline 4-ON, an amine compound, and a solvent mix and agitate in the atmosphere of inactive gas etc., for example. 20-200 degrees C of reaction temperature in that case is 40-150 degrees C still more preferably preferably, and reaction pressure in particular is not restricted.
In addition, the 6-alkoxy 7-amino alkoxy quinazoline 4-ON derivative of output or a 7-alkoxy 6-amino alkoxy quinazoline 4-ON derivative is after the end of a reaction. For example, it is isolated and refined by general methods, such as filtration, concentration, distillation, a re-crystal, ****, and a column chromatography.
Next, the work example of this invention is indicated.
[Work example I-1] (composition of 6-iodine quinazoline 4-ON)
1.00g (3.8mmmol) of 5-iodine anthranilic acid, ORUTOGI acid MECHIRU 0.81g (7.6mmmol), 0.59g (7.6mmmol) of ammonium acetate, and methanol 4.0mL were added to the resisting pressure container made from stainless steel of content volume 10mL, and it was made to react to it at 120 degrees C for 3 hours. It cooled to room temperature after the end of a reaction, after adding water 40mL to reaction liquid and making it agitate for 15 minutes, it filtered, and the 6-iodine quinazoline 4-ON 0.97g was obtained as a light gray crystal (isolation ****: 93%).
The physical-properties value of 6-iodine quinazoline 4-ON was as follows.
Melting point; 259 degrees C (decomposition)

1H-NMR(DMSO-d6, delta (ppm));7.46 (1H, d, J= 8.4Hz), 8.08-8.15 (2H, m), 8.39 (1H, d, J= 1.8Hz), 12.5 (1H, brs)
CI-MS(m/e);273(M+1)

[Work example I-2] (composition of 6-iodine quinazoline 4-ON)
In the work example I-1, it reacted like the work example I-1 except having changed the quantity of ORUTOGI acid MECHIRU into 1.61g (15.2mmmol), and having changed the quantity of ammonium acetate into 1.17g (15.2mmmol). As a result, 6-iodine quinazoline 4-ON was generating 0.98g (reaction ****: 94%).

[Work example I-3] (composition of 6-iodine quinazoline 4-ON)
In the work example I-2, the quantity of ORUTOGI acid MECHIRU was changed into 3.60g (34mmmol), and it reacted like the work example I-2 except not having used methanol. As a result, 6-iodine quinazoline 4-ON was generating 0.94g (reaction ****: 91%).

[Work example I-4] (composition of 6-iodine quinazoline 4-ON)
In the work example I-2, it reacted like the work example I-2 except having changed methanol into acetonitrile. As a result, 6-iodine quinazoline 4-ON was generating 0.98g (reaction ****: 94%).

[Work example I-5] (composition of 6-iodine quinazoline 4-ON)
In the work example I-2, it reacted like the work example I-2 except having changed ammonium acetate into 3.20g (15.2mmmol) of 2 and 4-dichloro ammonium benzoate. As a result, the 6-iodine quinazoline 4-ON 0.97g was generating (reaction ****: 90%).

[Work example I-6] (composition of 6-iodine quinazoline 4-ON)
In the work example I-2, it reacted like the work example I-2 except having changed ammonium acetate into 0.95g (15.2mmmol) of ammonium formate. Reaction liquid was processed like the work example I-1 after the end of a reaction, and the 6-iodine quinazoline 4-ON 0.88g was obtained as a light gray crystal (isolation ****: 85%).

[Work example I-7] (composition of 7-chloro quinazoline 4-ON)
1.00g (5.8mmmol) of 4-chloro anthranilic acid, ORUTOGI acid MECHIRU 2.47g (23.3mmmol), 1.80g (23.3mmmol) of ammonium acetate, and methanol 4.0mL were added to the resisting pressure container made from stainless steel of content volume 10mL, and it was made to react to it at 120 degrees C for 3 hours. It cooled to room temperature after the end of a reaction, after adding water 40mL to reaction liquid and making it agitate for 15 minutes, it filtered, and the 7-chloro quinazoline 4-ON 0.96g was obtained as a white crystal (isolation ****: 92%).
The physical-properties value of 7-chloro quinazoline 4-ON was as follows.
Melting point; 246-247 degrees C
1H-NMR(DMSO-d6, delta (ppm));7.56 (1H, dd, J= 1.8, 8.1Hz), 7.72 (1H, d, J= 1.8Hz), 8.10-8.14 (2H, m), 12.5 (1H, brs)
CI-MS(m/e);181(M+1)

[Work example I-8] (composition of 6-nitroglycerine quinazoline 4-ON)
1.00g (5.5mmmol) of 5-nitroglycerine anthranilic acid, ORUTOGI acid MECHIRU 2.33g (22.0mmmol), 1.69g (22.0mmmol) of ammonium acetate, and methanol 4.0mL were added to the resisting pressure container made from stainless steel of content volume 10mL, and it was made to react to it at 120 degrees C for 3 hours. It cooled to room temperature after the end of a reaction, after adding water 40mL to reaction liquid and making it agitate for 15 minutes, it filtered, and the 6-nitroglycerine quinazoline 4-

ON 0.91g was obtained as a yellow crystal (isolation ****: 87%). The physical-properties value of 6-nitroglycerine quinazoline 4-ON was as follows. Melting point; 277-278 degrees C 1H-NMR(DMSO-d6, delta (ppm));7.87 (1H, d, J= 9.0Hz), 8.32 (1H, s), 8.55 (1H, dd, J= 2.7, 9.0Hz), 8.81 (1H, d, J= 2.7Hz), 12.5 (1H, brs) CI-MS(m/e);192(M+1)

[Work example I-9] (composition of 6 and 7-dimethoxy quinazoline 4-ON) To the resisting pressure container made from stainless steel of content volume 10mL, they are 4 and 1.00g (5.1mmmol) of 5-dimethoxy anthranilic acid, ORUTOGI acid MECHIRU 2.15g (20.3mmmol), 1.56g (20.3mmmol) of ammonium acetate, and methanol 4.0mL were added, and it was made to react at 120 degrees C for 3 hours. It cooled to room temperature after the end of a reaction, after adding water 40mL to reaction liquid and making it agitate for 15 minutes, it filtered, and the 6 and 7-dimethoxy quinazoline 4-ON 0.96g was obtained as a brown crystal (isolation ****: 92%). The physical-properties value of 6 and 7-dimethoxy quinazoline 4-ON was as follows. Melting point; 294-295 degrees C 1H-NMR(DMSO-d6, delta (ppm));3.87 (3H, s), 3.90 (3H, s), 7.13 (1H, s), 7.44 (1H, s), 7.99 (1H, s), 12.5 (1H, brs) CI-MS(m/e);207(M+1)

[Work example I-10] (composition of 6-nitroglycerine 7-chloro quinazoline 4-ON) To the resisting pressure container made from stainless steel of content volume 10mL, it is 0.94g (4.3mmmol) of 4-chloro 5-nitroglycerine anthranilic acid, ORUTOGI acid MECHIRU 1.96g (18.5mmmol), 1.42g (18.5mmmol) of ammonium acetate, and methanol 4.0mL were added, and it was made to react at 120 degrees C for 4 hours. It cooled to room temperature after the end of a reaction, after adding water 40mL to reaction liquid and making it agitate for 15 minutes, it filtered, and the 6-nitroglycerine 7-chloro quinazoline 4-ON 0.88g was obtained as a yellow crystal (isolation ****: 90%). The physical-properties value of 6-nitroglycerine 7-chloro quinazoline 4-ON was as follows.

Melting point; 300 degrees C (decomposition) 1H-NMR(DMSO-d6, delta (ppm));8.03 (1H, s), 8.32 (1H, s), 8.69 (1H, s), 12.5 (1H, brs) CI-MS(m/e);226(M+1)

[Work example I-11] (composition of 6-hydroxy quinazoline 4-ON) To the resisting pressure container made from stainless steel of content volume 10mL, it is 1.00g (6.6mmmol) of 5-hydroxy anthranilic acid, ORUTOGI acid MECHIRU 2.80g (26.4mmmol), 2.00g (26.4mmmol) of ammonium acetate, and methanol 4.0mL were added, and it was made to react at 120 degrees C for 3 hours. It cooled to room temperature after the end of a reaction, after adding water 40mL to reaction liquid and making it agitate for 15 minutes, it filtered, and the 6-hydroxy quinazoline 4-ON 0.78g was obtained as a light gray crystal (isolation ****: 74%). The physical-properties value of 6-hydroxy quinazoline 4-ON was as follows. Melting point; 332-333 degrees C (decomposition) 1H-NMR(DMSO-d6, delta (ppm));7.25 (1H, dd, J= 2.7, 8.7Hz), 7.41 (1H, d, J= 2.7Hz), 7.53 (1H, d, J= 8.7Hz), 7.90 (1H, s), 12.6 (2H, brs) CI-MS(m/e);163(M+1)

[Work example I-12] (composition of 6-KARUBOKISHI quinazoline 4-ON)

To the resisting pressure container made from stainless steel of content volume 10mL, it is 1.00g (5.5mmmol) of 5-KARUBOKI cyanogen truck nil acid, ORUTOGI acid MECHIRU 2.30g (22.0mmmol), 1.70g (22.0mmmol) of ammonium acetate, and methanol 4.0mL were added, and it was made to react at 120 degrees C for 3 hours. It cools to room temperature after the end of a reaction, after adding water 40mL, and 1mol / L chloride 10mL to reaction liquid and making it agitate for 15 minutes, it filters, and it is a yellow crystal. The 91% (area percentage by high speed liquid chromatography) of purity 6-KARUBOKISHI quinazoline 4-ON 0.96g was obtained (isolation ****: 84%). The physical-properties value of 6-KARUBOKISHI quinazoline 4-ON was as follows. 1H-NMR(DMSO-d6, delta (ppm));3.93 (1H, brs), 8.01 (1H, dd, J= 1.5, 7.8Hz), 8.17 (1H, d, J= 1.5Hz), 8.22 (1H, d, J= 7.8Hz), 8.28 (1H, s), 12.0 (1H, brs) CI-MS(m/e);191(M+1)

[Work example I-13] (composition of quinazoline 4-ON) 302mg (2.0mmmol) of methyl anthranilate and ORUTOGI acid MECHIRU424mg (4.0mmmol), 308mg (4.0mmmol) of ammonium acetate, and methanol 1.0mL were added to the resisting pressure container made from stainless steel of content volume 2mL, and it was made to react to it at 120 degrees C for 3 hours. After the end of a reaction, when high speed liquid chromatography analyzed reaction liquid (absolutely determination method), quinazoline 4-ON was generating 285mg (reaction ****: 98%).

[Work example I-14] (composition of quinazoline 4-ON) In the work example I-13, it reacted like the work example I-13 except having changed methanol into acetonitrile. As a result, quinazoline 4-ON was generating 277mg (reaction ****: 95%).

[Work example I-15] (composition of quinazoline 4-ON) In the work example I-13, it reacted like the work example I-13 except having changed methanol into N and N'-JIMECHIRU imidazolidinone. As a result, quinazoline 4-ON was generating 267mg (reaction ****: 91%).

[Work example I-16] (composition of 6-nitroglycerine 7-(3-hydroxy propoxy) quinazoline 4-ON)

To the resisting pressure container made from stainless steel of content volume 10mL, they are 0.65g (2.5mmmol) of 5-nitroglycerine 4-(3-hydroxy propoxy) anthranilic acid, ORUTOGI acid MECHIRU 1.06g (10.0mmmol), 0.77g (10.0mmmol) of ammonium acetate, and methanol 6.0mL. It was made to react at 140 degrees C in addition for 6.5 hours. Cooled to room temperature after the end of a reaction, and filtered the crystal which added water 50mL to reaction liquid, and deposited, it was made to dry under decompression, and the 6-nitroglycerine 7-(3-hydroxy propoxy) quinazoline 4-ON 0.52g was obtained as a gray crystal (isolation ****: 79%). The physical-properties value of 6-nitroglycerine 7-(3-hydroxy propoxy) quinazoline 4-ON was as follows. 1H-NMR(DMSO-d6, delta (ppm));1.86-1.95 (2H, m), 3.57 (2H, t, J= 6.0Hz), 4.34 (2H, t, J= 6.0Hz), 7.42 (1H, s), 8.22 (1H, s), 8.53 (1H, s) CI-MS(m/e);266(M+1)

[Work example I-17] (composition of 6-nitroglycerine 7-hydroxy quinazoline 4-ON) To the resisting pressure container made from stainless steel of content volume 10mL, it is 0.50g (7.5mmmol) of 5-nitroglycerine 4-hydroxy anthranilic acid, ORUTOGI acid MECHIRU 0.80g (7.5mmmol), 0.58g (7.5mmmol) of ammonium acetate, and methanol

5.0mL were added, and it was made to react at 120 degrees C for 3 hours. After cooling to room temperature after the end of a reaction and distilling off methanol under decompression, water 5mL was added to reaction liquid. Filtered the crystal which deposited, it was made to dry under decompression, and the 6-nitroglycerine 7-hydroxy quinazoline 4-ON 0.29g was obtained as a yellow crystal (isolation ****: 55%). The physical-properties value of 6-nitroglycerine 7-hydroxy quinazoline 4-ON was as follows.

1H-NMR(DMSO-d6, delta (ppm));3.38 (1H, brs), 7.20 (1H, s), 8.15 (1H, s), 8.53 (1H, s) CI-MS(m/e);208(M+1)

[Work example I-18] (composition of 6 and 7-bis(2-methoxyethoxy) quinazoline 4-ON) To the resisting pressure container made from stainless steel of content volume 10mL, they are 4, 1.00g (2.8mmmol) of 5-bis(2-methoxyethoxy) anthranilic acid, ORUTOGI acid MECHIRU 0.93g (8.8mmmol), 0.67g (8.8mmmol) of ammonium acetate, and methanol 5.0mL. It was made to react at 95 degrees C in addition for 8 hours. It cooled to room temperature after the end of a reaction, and reaction liquid was condensed under decompression. Subsequently, the concentration thing was re-crystallized by methanol 20mL. It was made to dry under decompression after filtering a crystal, and the 6 and 7-bis(2-methoxyethoxy) quinazoline 4-ON 0.85g was obtained as a white crystal (isolation ****: 83%).

The physical-properties value of 6 and 7-bis(2-methoxyethoxy) quinazoline 4-ON was as follows.

1H-NMR(D2O, delta (ppm));3.49 (3H, s), 3.50 (3H, s), 3.86-3.88 (4H, m), 3.97 (2H, d, J= 3.6Hz), 4.04 (2H, d, J= 3.6Hz), 6.41 (1H, s), 6.72 (1H, s), 7.72 (1H, s) CI-MS(m/e);295(M+1)

[Work example 1-19] (composition of 6 and 7-bis(2-methoxyethoxy) quinazoline 4-ON) To the resisting pressure container made from stainless steel of content volume 10mL, they are 4, 5-bis(2-methoxyethoxy) anthranilic acid ethyl 1.02g (3.3mmmol), ORUTOGI acid MECHIRU 0.96g (9.1mmmol), 0.69g (9.1mmmol) of ammonium acetate, and methanol 5.0mL. It was made to react at 110 degrees C in addition for 6 hours. It cooled to room temperature after the end of a reaction, and reaction liquid was condensed under decompression. Subsequently, the concentration thing was re-crystallized by methanol 20mL. It was made to dry under decompression after filtering a crystal, and the 6 and 7-bis(2-methoxyethoxy) quinazoline 4-ON 0.87g was obtained as a white crystal (isolation ****: 91%).

[Work example I-20] (composition of 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON)

In the resisting pressure container made from stainless steel of content volume 100mL, 5.80g (17.9mmmol) of 5-********- 4-(3-morpholino propoxy) methyl anthranilate, ORUTOGI acid MECHIRU 3.79g (35.8mmmol), 2.56g (33.2mmmol) of ammonium acetate, and methanol 30mL It was made to react at 115 degrees C in addition for 5 hours. It cooled to room temperature after the end of a reaction, and reaction liquid was condensed under decompression. Subsequently, the concentration thing was re-crystallized by methanol 100mL. It was made to dry under decompression after filtering a crystal, and the 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON 4.97g was obtained as a white crystal (isolation ****: 87%).

The physical-properties value of 6-********- 7-(3-morpholino propoxy) quinazoline 4-

ON was as follows.
1H-NMR(DMSO-d6, delta (ppm));2.08-2.13 (2H, m), 2.48 (4H, t, J= 4.5Hz), 2.56 (2H, t, J= 6.9Hz), 3.73 (4H, t, J= 4.5Hz), 4.00 (3H, s), 4.24 (2H, t, J= 6.6Hz), 7.18 (1H, s), 7.60 (1H, s), 8.02 (1H, s), 10.5 (1H, brs)
CI-MS(m/e);320(M+1)
[Work example I-21] (composition of 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON)
In the resisting pressure container made from stainless steel of content volume 10mL, 1.00g (3.1mmmol) of 5-********- 4-(3-piperidino propoxy) methyl anthranilate, ORUTOGI acid MECHIRU 0.99g (9.3mmmol), 0.72g (9.3mmmol) of ammonium acetate, and methanol 5.0mL It was made to react at 120 degrees C in addition for 5 hours. When it cooled to room temperature after the end of a reaction and reaction liquid was analyzed by high speed liquid chromatography (absolutely determination method), the 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON 0.89g was generating (reaction ****: 90%).
[Work-example II-1] (composition of 4-(2-chloroethoxy)-3-METOKISHI methyl benzoate)
It is 1.00g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the reflux condenser, 0.85g (6.04mmmol) of potassium carbonate and acetonitrile 30mL of the 2-bromo 1-chloro ethane 1.04g (7.14mmmol) of purity 98 mass % and purity 98 mass % are added, and it was made to react for 8 hours, agitating under flowing back (80-85 degrees C) in argon atmosphere. After the end of a reaction, after filtering reaction liquid, it condenses under decompression, and subsequently, n-Cheb Than 20mL was added and the crystal was deposited. It was made to dry under decompression after filtering a crystal, and 1.34g of 4-(2-chloroethoxy)-3-METOKISHI methyl benzoate of 98% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 97.8%).
The physical-properties value of 4-(2-chloroethoxy)-3-METOKISHI methyl benzoate was as follows.
Melting point; 61-62 degrees C
1H-NMR(CDCl3, delta (ppm));3.65-3.69 (2H, m), 3.82 (3H, s), 3.90 (3H, s), 4.35 (2H, t, J= 3.0Hz), 6.95 (1H, d, J= 6.0Hz), 7.57 (1H, s), 7.67 (1H, d, J= 6.0Hz)
[Work-example II-2] (composition of 4-(2-chloroethoxy)-5-********- 2-nitroglycerine methyl benzoate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 1.02g (4.09mmmol) of 4-(2-chloroethoxy)-3-METOKISHI methyl benzoate and 0.03g (0.40mmmol) of sodium nitrite of 98% of the purity compounded by work-example II-1, and acetic acid 1.25mL. It heated. Subsequently, 1.72g (16.5mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at 40-50 degrees C for 5 hours. After the end of a reaction, when water 5mL was added and it cooled to 20 degrees C, the crystal deposited. After washing by water 5mL, it was made to dry under decompression after filtering a crystal, and 1.12g of 4-(2-chloroethoxy)-5-********- 2-nitroglycerine methyl benzoate of 98% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 93.0%).

The physical-properties value of 4-(2-chloroethoxy)-5-********- 2-nitroglycerine methyl benzoate was as follows.
Melting point; 116-117 degrees C
1H-NMR(CDCl3, delta (ppm));3.65-3.69 (2H, m), 3.90 (3H, s), 3.91 (3H, s), 4.35 (2H, t, J= 6.0Hz), 7.09 (1H, s), 7.49 (1H, s)
[Work-example II-3] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate)
It is 1.02g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, 0.85g (6.04mmmol) of potassium carbonate and acetonitrile 30mL of the 3-bromo 1-chloro propane 1.15g (7.14mmmol) of purity 98 mass % and purity 98 mass % are added, and it was made to react for 8 hours, agitating under flowing back (80-85 degrees C) in argon atmosphere. After the end of a reaction, after filtering reaction liquid, it condenses, and subsequently, n-Cheb Than was added and the crystal was deposited. It was made to dry under decompression after filtering a crystal, and 1.34g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 97.8%).
The physical-properties value of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was as follows.
Melting point; 98-99 degrees C
1H-NMR(CDCl3, delta (ppm));2.27-2.35 (2H, m), 3.75-3.79 (2H, m), 3.85 (3H, s), 3.91 (3H, s), 4.22 (2H, t, J= 6.0Hz), 6.95 (1H, d, J= 6.0Hz), 7.57 (1H, s), 7.67 (1H, d, J= 6.0Hz)
[Work-example II-4] (composition of 4-(3-chloro propoxy)-5-********- 2-nitroglycerine methyl benzoate)
[the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C - 50 degrees C, adding and agitating 10.1g (38.7mmmol) of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate and the sodium nitrite 0 and 27g (3.87mmmol) of 99% of the purity compounded by the same method as work-example II-3, and acetic acid 12.5mL. It heated. Subsequently, 16.2g (154.8mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at this temperature for 5 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing in order of water 30mL and n-Cheb Than 30mL, it is made to dry under decompression after filtering a crystal, and it is a white crystal, 10.9g of 4-(3-chloro propoxy)-5-********- 2-nitroglycerine methyl benzoate of 98% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 92.0%).
The physical-properties value of 4-(3-chloro propoxy)-5-********- 2-nitroglycerine methyl benzoate was as follows.
Melting point; 63-64 degrees C
1H-NMR(CDCl3, delta (ppm));2.29-2.37 (2H, m), 3.67-3.79 (2H, m), 3.87 (3H, s), 3.96 (3H, s), 7.08 (1H, s), 7.50 (1H, s)
[Work-example II-5] (composition of 4-(3-chloro propoxy)-5-********- 2-nitroglycerine methyl benzoate)
It is 3-bromo 1-chloro propane 11.2g (71.4mmmol) of purity 98 mass % to the glass

flasks of content volume 200mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, 8.52g (60.4mmmol) of potassium carbonate and acetone 40mL of purity 98 mass % are added, and it was made to flow back, agitating in argon atmosphere (52-57 degrees C). Subsequently, it was dropped gently, having covered the solution which dissolved 10.2g (54.9mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % in acetone 40mL for 30 minutes, and it was made to react at this temperature for 5 hours. Reaction liquid was filtered after the end of a reaction, it condensed under decompression of ****, and 17.0g of solution which mainly contains 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was obtained. Subsequently, be mainly concerned with the 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate obtained previously in the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, and the tap funnel. It heated to 40 degrees C - 50 degrees C, adding and agitating 14.0g of solution, 0.20g (2.60mmmol) of sodium nitrite, and acetic acid 17.5mL which are included. Subsequently, 22.4g (215.2mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at this temperature for 2 hours. After the end of a reaction, warm water 42mL was added, the organic layer was separated, and warm water washed. When this organic layer was analyzed in high speed liquid chromatography (absolutely determination method), 15.7g of 4-(3-chloro propoxy)-5-********- 2-nitroglycerine methyl benzoate was generating (reaction ****: 96.2%).

[Work-example II-6] (composition of 4-(3-chloro propoxy)-5-********- 2-nitroglycerine methyl benzoate)

It is 3-bromo 1-chloro propane 105.9g (659mmmol) of purity 98 mass % to glass flasks with an equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser content volume of 1l., 58.1g (411mmmol) of potassium carbonate and acetone 300mL of purity 98 mass % are added, and it was made to flow back, agitating in argon atmosphere (52-57 degrees C). Subsequently, it was dropped gently, having covered the solution which dissolved 51.0g (274mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % in acetone 200mL for 30 minutes, and it was made to react at this temperature for 2 hours. Reaction liquid was filtered after the end of a reaction, it condensed under decompression of ****, and 138.0g of 3-bromo 1-chloro propane solution which mainly contains 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was obtained.

Subsequently, be mainly concerned with the 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate obtained previously in the glass flasks of content volume 500mL equipped with churning equipment, the thermometer, and the tap funnel. It heated even at 40 degrees C - 50 degrees C, adding and agitating 138.0g of 3-bromo 1-chloro propane solution, 0.93g (13.7mmmol) of sodium nitrite, and acetic acid 90mL which are included. Subsequently, 111.5g (215.2mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at this temperature for 2 hours. After the end of a reaction, warm water 210mL was added, the organic layer was separated, and it washed by warm water 210mL. When this organic layer was analyzed in high speed liquid chromatography (absolutely determination method), 78.7g of 4-(3-chloro propoxy)-5-********- 2-nitroglycerine methyl benzoate was generating (reaction ****: 94.5%).

[Work-example II-7] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate)

It is 1.02g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, 1.16g (8.24mmmol) of potassium carbonate and acetonitrile 10mL of the 3-bromo 1-chloro propane 2.12g (13.2mmmol) of purity 98 mass % and purity 98 mass % are added, and it was made to react for 5 hours, agitating under flowing back (80-85 degrees C) in argon atmosphere. When reaction liquid was filtered after the end of a reaction and **** was analyzed in high speed liquid chromatography (absolutely determination method), 1.38g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was generating (reaction ****: 97.0%).
[Work-example II-8] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate) Churning equipment, [the glass flasks of content volume 50mL equipped with the thermometer, the tap funnel, and the reflux condenser] 1.02g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass %, While adding 1.16g (8.24mmmol) of potassium carbonate and acetonitrile 10mL of the 3-bromo 1-chloro propane 3.17g (19.8mmmol) of purity 98 mass %, and purity 98 mass % and agitating under flowing back (80-85 degrees C) in argon atmosphere It was made to react for 5 hours. When reaction liquid was filtered after the end of a reaction and **** was analyzed in high speed liquid chromatography (absolutely determination method), 1.41g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was generating (reaction ****: 98.9%).
[Work-example II-9] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate)
It is 1.02g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, 1.16g (8.24mmmol) of potassium carbonate and methyl-ethyl-ketone 10mL of the 3-bromo 1-chloro propane 2.12g (13.2mmmol) of purity 98 mass % and purity 98 mass % are added, and it was made to react for 2 hours, agitating under flowing back (77-82 degrees C) in argon atmosphere. When reaction liquid was filtered after the end of a reaction and **** was analyzed in high speed liquid chromatography (absolutely determination method), 1.36g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was generating (reaction ****: 95.4%).
[Work-example II-10] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate)
It is 1.02g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, 1.16g (8.24mmmol) of potassium carbonate and methanol 30mL of the 3-bromo 1-chloro propane 2.12g (13.2mmmol) of purity 98 mass % and purity 98 mass % are added, and it was made to react for 10 hours, agitating under flowing back (62-67 degrees C) in argon atmosphere. When reaction liquid was filtered after the end of a reaction and **** was analyzed in high speed liquid chromatography (absolutely determination method), 1.23g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was generating (reaction ****: 86.5%).
[Work-example II-11] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate)
It is 1.02g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the

thermometer, the tap funnel, and the reflux condenser, 1.16g (8.24mmmol) of potassium carbonate [of the 3-bromo 1-chloro propane 2.12g (13.2mmmol) of purity 98 mass % and purity 98 mass %] and N, and N-JIMECHIRUHORUMU amide 10mL is added, and it was made to react at 52-57 degrees C for 5 hours, agitating in argon atmosphere. When reaction liquid was filtered after the end of a reaction and **** was analyzed in high speed liquid chromatography (absolutely determination method), 0.85g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was generating (reaction ****: 59.8%).
[Work-example II-12] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate)
It is 1.02g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, 1.16g (8.24mmmol) of potassium carbonate and acetone 10mL of the 3-bromo 1-chloro propane 2.12g (13.2mmmol) of purity 98 mass % and purity 98 mass % are added, and it was made to react for 5 hours, agitating under flowing back (55-60 degrees C) in argon atmosphere. When reaction liquid was filtered after the end of a reaction and **** was analyzed in high speed liquid chromatography (absolutely determination method), 1.38g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was generating (reaction ****: 97.2%).
[Work-example II-13] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate)
It is 1.02g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, The 3-bromo 1-chloro propane 2.12g (13.2mmmol) of purity 98 mass %, 1.16g (8.24mmmol) of potassium carbonate, acetone 5mL, and acetonitrile 5mL of purity 98 mass % are added, and it was made to react for 5 hours, agitating under flowing back (70-75 degrees C) in argon atmosphere. When reaction liquid was filtered after the end of a reaction and **** was analyzed in high speed liquid chromatography (absolutely determination method), 1.41g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was generating (reaction ****: 99.3%).
[Work-example II-14] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate)
It is 1.02g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, The 3-bromo 1-chloro propane 2.12g (13.2mmmol) of purity 98 mass %, 1.16g (8.24mmmol) of potassium carbonate, 1.02g (13.7mmmol) of potassium chloride, and acetone 10mL of purity 98 mass % are added, and it was made to react for 10 hours, agitating under flowing back (55-60 degrees C) in argon atmosphere. When reaction liquid was filtered after the end of a reaction and **** was analyzed in high speed liquid chromatography (absolutely determination method), 1.39g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was generating (reaction ****: 98.2%).
[Work-example II-15] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate)
It is 1.02g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, The 3-bromo 1-chloro propane

2.12g (13.2mmmol) of purity 98 mass %, 1.16g (8.24mmmol) of potassium carbonate, 1.02g (17.5mmmol) of sodium chloride, and acetone 10mL of purity 98 mass % are added, and it was made to react for 10 hours, agitating under flowing back (55-60 degrees C) in argon atmosphere. When reaction liquid was filtered after the end of a reaction and **** was analyzed in high speed liquid chromatography (absolutely determination method), 1.41g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was generating (reaction ****: 99.5%).

[Work-example II-16] (composition of 4-(3-bromo propoxy)-3-METOKISHI methyl benzoate)

It is 10.2g (54.9mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, 8.5g (60.4mmmol) of potassium carbonate and acetonitrile 30mL of 1 of purity 99 mass %, 3-dibromopropane 12.5g (60.4mmmol), and purity 98 mass % are added, and it was made to react for 8 hours, agitating under flowing back (80-85 degrees C) in argon atmosphere. After the end of a reaction, after filtering reaction liquid, it condensed under decompression. A concentration thing is refined by silica gel column chromatography (bulking agent; WAKOGERU C-200, developing solvent; n-hexane), and it is a white crystal, 15.1g of 4-(3-bromo propoxy)-3-METOKISHI methyl benzoate of 98% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 88.8%).

The physical-properties value of 4-(3-bromo propoxy)-3-METOKISHI methyl benzoate was as follows.

Melting point; 65-66 degrees C

1H-NMR(CDCl3, delta (ppm));2.01-2.43 (2H, m), 3.61-3.65 (2H, m), 3.89 (3H, s), 3.93 (3H, s), 4.19 (2H, t, J= 6.0Hz), 6.90 (1H, d, J= 6.0Hz), 7.55 (1H, s), 7.67 (1H, d, J= 6.0Hz)

[Work-example II-17] (composition of 5-********- 4-(3-bromo propoxy)-2-nitroglycerine methyl benzoate)

[the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 10.2g (33.0mmmol) of 4-(3-bromo propoxy)-3-METOKISHI methyl benzoate and 0.23g (3.30mmmol) of sodium nitrite of 98% of the purity compounded by work-example II-16, and acetic acid 12.5mL. It heated. Subsequently, 13.8g (132.0mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at 40 degrees C - 50 degrees C for 5 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing in order of water 30mL and n-Cheb Than 30mL, it is made to dry under decompression after filtering a crystal, and it is a white crystal, 10.7g of 5-********- 4-(3-bromo propoxy)-2-nitroglycerine methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 92.0%).

The physical-properties value of 5-********- 4-(3-bromo propoxy)-2-nitroglycerine methyl benzoate was as follows.

Melting point; 71-72 degrees C

1H-NMR(CDCl3, delta (ppm));2.37-2.45 (2H, m), 3.60-3.66 (2H, m), 3.90 (3H, s), 3.96 (3H, s), 7.08 (1H, s), 7.50 (1H, s)

[Work-example II-18] (composition of 4-(4-chloro butoxy)-3-METOKISHI methyl

benzoate)
It is 10.2g (54.9mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, and the reflux condenser, 8.5g (60.4mmmol) of potassium carbonate and acetonitrile 300mL of the 4-bromo 1-chloro butane 12.6g (71.4mmmol) of purity 99 mass % and purity 98 mass % are added, and it was made to react for 8 hours, agitating under flowing back (80-85 degrees C) in argon atmosphere. After the end of a reaction, after filtering reaction liquid, it condenses under decompression, and a concentration thing is refined by silica gel column chromatography (bulking agent; WAKOGERU C-200, developing solvent; n-hexane), and it is a colorless liquid, 13.6g of 4-(4-chloro butoxy)-3-METOKISHI methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 90.0%).

Continued translation.

4-(4-chloro butoxy)-3-METOKISHI methyl benzoate is a new molecular entity shown with the following physical-properties values.
1H-NMR(CDCl3, delta (ppm));1.96-2.07 (4H, m), 3.61-3.67 (2H, m), 3.89 (3H, s), 3.93 (3H, s), 4.13 (2H, t, J= 6.0Hz), 6.87 (1H, d, J= 6.0Hz), 7.55 (1H, s), 7.64 (1H, d, J= 7Hz)
[Work-example II-19] (composition of 5-********- 4-(4-chloro butoxy)-2-nitroglycerine methyl benzoate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 10.1g (36.7mmmol) of 4-(4-chloro butoxy)-3-METOKISHI methyl benzoate and 0.25g (3.67mmmol) of sodium nitrite of 99% of the purity compounded by work-example II-18, and acetic acid 12.5mL. It heated. Subsequently, 115.4g (146.8mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at 40 degrees C - 50 degrees C for 5 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing in order of water 30mL and n-Cheb Than 30mL, it is made to dry under decompression after filtering a crystal, and it is a white crystal, 10.9g of 5-********- 4-(4-chloro butoxy)-2-nitroglycerine methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 92.0%).
5-********- 4-(4-chloro butoxy)-2-nitroglycerine methyl benzoate is a new molecular entity shown with the following physical-properties values.
Melting point; 74-75 degrees C
1H-NMR(CDCl3, delta (ppm));1.95-2.10 (4H, m), 3.61-3.66 (2H, m), 3.89 (3H, s), 3.93 (3H, s), 4.13 (2H, t, J= 6.0Hz), 6.87 (1H, d, J= 6.0Hz), 7.26 (1H, s), 7.44 (1H, s)
[Work-example II-20] (composition of 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate)
It is 10.2g (54.9mmmol) of 3-hydroxy 4-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, and the reflux condenser, 8.5g (60.4mmmol) of potassium carbonate and acetone 30mL of the 3-bromo 1-chloro propane 11.5g (71.4mmmol) of purity 98 mass %

and purity 98 mass % are added, and it was made to react for 8 hours, agitating under flowing back (80-85 degrees C) in argon atmosphere. Reaction liquid was filtered after the end of a reaction, n-Cheb Than was added to the concentration thing, and the crystal was deposited. After filtering a crystal, it was made to dry under decompression, and 13.7g of 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 95.8%).

The physical-properties value of 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate was as follows.

Melting point; 46-48 degrees C

1H-NMR(CDCl3, delta (ppm));2.27-2.33 (2H, m), 3.64-3.75 (2H, m), 3.79 (3H, s), 3.91 (3H, s), 4.21 (2H, t, J= 5.0Hz), 6.88 (1H, d, J= 6.0Hz), 7.67 (1H, d, J= 6.0Hz), 7.58 (1H, s), 7.70 (1H, d, J= 6.0Hz)

[Work-example II-21] (composition of 4-*********- 5-(3-chloro propoxy)-2-nitroglycerine methyl benzoate)

[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 10.1g (38.7mmmol) of 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate and 0.27g (3.87mmmol) of sodium nitrite of 99% of the purity compounded by work-example II-20, and acetic acid 12.5mL. It heated. Subsequently, 16.2g (154.8mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at 40 degrees C - 50 degrees C for 5 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing in order of water 30mL and n-Cheb Than 30mL, it is made to dry under decompression after filtering a crystal, and it is a white crystal, 11.3g of 4-*********- 5-(3-chloro propoxy)-2-nitroglycerine methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 95.0%).

The physical-properties value of 4-*********- 5-(3-chloro propoxy)-2-nitroglycerine methyl benzoate was as follows.

Melting point; 63-64 degrees C

1H-NMR(CDCl3, delta (ppm));2.28-2.37 (2H, m), 3.64-3.75 (2H, m), 3.89 (3H, s), 3.99 (3H, s), 4.24 (2H, t, J= 5.0Hz), 7.11 (1H, s), 7.45 (1H, s)

[Example IIIof reference-1] (composition of 4-(2-chloroethoxy)-3-METOKISHI methyl benzoate)

It is 1.00g (5.49mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the reflux condenser, 2-bromo 1-chloro ethane 1.02g (7.14mmmol), 0.83g (6.04mmmol) of potassium carbonate, and acetonitrile 30mL are added, and it was made to react for 8 hours, agitating under flowing back (80-85 degrees C) in argon atmosphere. After the end of a reaction, after filtering reaction liquid, it condenses under decompression, and subsequently, n-Cheb Than 20mL was added and the crystal was deposited. It was made to dry under decompression after filtering a crystal, and 1.34g of 4-(2-chloroethoxy)-3-METOKISHI methyl benzoate of 98% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 97.8%).

The physical-properties value of 4-(2-chloroethoxy)-3-METOKISHI methyl benzoate

was as follows.
Melting point; 61-62 degrees C
1H-NMR(CDCl3, delta (ppm));3.65-3.69 (2H, m), 3.82 (3H, s), 3.90 (3H, s), 4.35 (2H, t, J= 3.0Hz), 6.95 (1H, d, J= 6.0Hz), 7.57 (1H, s), 7.67 (1H, d, J= 6.0Hz)
[Example IIIof reference-2] (composition of 5-********- 4-(2-chloroethoxy)-2-nitroglycerine methyl benzoate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 1.02g (4.08mmmol) of 4-(2-chloroethoxy)-3-METOKISHI methyl benzoate and 0.03g (0.40mmmol) of sodium nitrite of 98% of the purity compounded by example IIIof reference-1, and acetic acid 1.25mL. It heated. Subsequently, 1.72g (16.5mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at this temperature for 5 hours. After the end of a reaction, when water 5mL was added and it cooled to 20 degrees C, the crystal deposited. After washing by water 5mL, it was made to dry under decompression after filtering a crystal, and 1.12g of 5-********- 4-(2-chloroethoxy)-2-nitroglycerine methyl benzoate of 98% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 93.0%).
The physical-properties value of 5-********- 4-(2-chloroethoxy)-2-nitroglycerine methyl benzoate was as follows.
Melting point; 116-117 degrees C
1H-NMR(CDCl3, delta (ppm));3.65-3.69 (2H, m), 3.90 (3H, s), 3.91 (3H, s), 4.35 (2H, t, J= 6.0Hz), 7.09 (1H, s), 7.49 (1H, s)
[Work-example III-1] (composition of 5-********- 4-(2-chloroethoxy) methyl anthranilate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the reflux condenser, and the gas introduction pipe] It is 50 degrees C, adding and agitating 1.02g (3.45mmmol) of 5-********- 4-(2-chloroethoxy)-2-nitroglycerine methyl benzoate and methanol 20mL of 98% of purity which were compounded in example IIIof reference-2. It heated. Subsequently, it was made to react at this temperature for 1 hour, blowing hydrogen at the rate of . by 50mL/under normal pressure, after adding 3 mass % sulfuration platinum / 0.5g of carbon (65.7% water article) at this temperature. After the end of a reaction, when it condensed under decompression after filtering reaction liquid, the crystal deposited. It was made to dry under decompression of the obtained crystal, and 0.91g of 5-********- 4-(2-chloroethoxy) methyl anthranilate of 99% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 93.0%).
The physical-properties value of 5-********- 4-(2-chloroethoxy) methyl anthranilate was as follows.
Melting point; 112-113 degrees C
1H-NMR(CDCl3, delta (ppm));3.77 (3H, s), 3.79 (3H, s), 3.81-3.92 (2H, m), 4.25 (2H, t, J= 6.0Hz), 5.56 (2H, brs), 6.15 (1H, s), 7.34 (1H, s)
[Example IIIof reference-3] (composition of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate)
It is 10.2g (54.9mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, 3-bromo 1-chloro propane 11.2g

(71.4mmmol), 8.3g (60.4mmmol) of potassium carbonate, and acetonitrile 30mL are added, and it was made to react for 8 hours, agitating under flowing back (80-85 degrees C) in argon atmosphere. After the end of a reaction, after filtering reaction liquid, it condenses, and subsequently, n-Cheb Than was added and the crystal was deposited. It was made to dry under decompression after filtering a crystal, and 14.0g of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 97.8%).
The physical-properties value of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate was as follows.
Melting point; 98-99 degrees C
1H-NMR(CDCl3, delta (ppm));2.27-2.35 (2H, m), 3.75-3.79 (2H, m), 3.85 (3H, s), 3.91 (3H, s), 4.22 (2H, t, J= 6.0Hz), 6.95 (1H, d, J= 6.0Hz), 7.57, (1H, s), 7.67 (1H, d, J= 6.0Hz)
[Example IIIof reference-4] (composition of 5-*********- 4-(3-chloro propoxy)-2-nitroglycerine methyl benzoate)
[the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 10.1g (38.7mmmol) of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate and 0.27g (3.87mmmol) of sodium nitrite of 99% of the purity compounded by example IIIof reference-3, and acetic acid 12.5mL. It heated. Subsequently, 16.2g (154.8mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at this temperature for 5 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing in order of water 30mL and n-Cheb Than 30mL, it is made to dry under decompression after filtering a crystal, and it is a white crystal, 10.9g of 5-*********- 4-(3-chloro propoxy)-2-nitroglycerine methyl benzoate of 98% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 92.0%).
The physical-properties value of 5-*********- 4-(3-chloro propoxy)-2-nitroglycerine methyl benzoate was as follows.
Melting point; 63-64 degrees C
1H-NMR(CDCl3, delta (ppm));2.29-2.37 (2H, m), 3.67-3.79 (2H, m), 3.87 (3H, s), 3.96 (3H, s), 7.08 (1H, s), 7.50 (1H, s)
[Work-example III-2] (composition of 5-*********- 4-(3-chloro propoxy) methyl anthranilate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the reflux condenser, and the gas introduction pipe] It is 40 degrees C, adding and agitating 2.02g (6.58mmmol) of 5-*********- 4-(3-chloro propoxy)-2-nitroglycerine methyl benzoate and methanol 40mL of 99% of purity which were compounded in example IIIof reference-4. It heated. Subsequently, it was made to react at this temperature for 2 hours, blowing hydrogen the speed for 50mL/under normal pressure, after adding 5 mass % palladium / 0.2g of carbon (49% water article) at this temperature. After the end of a reaction, when it condensed under decompression after filtering reaction liquid, the crystal deposited. It was made to dry under decompression of the obtained crystal, and 1.79g of 5-*********- 4-(3-chloro propoxy) methyl anthranilate of 98% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 98.1%).

The physical-properties value of 5-********- 4-(3-chloro propoxy) methyl anthranilate was as follows.
Melting point; 98-99 degrees C
1H-NMR(CDCl3, delta (ppm));2.26-2.33 (2H, m), 2.73-2.76 (2H, m), 3.80 (3H, s), 3.84 (3H, s), 4.13 (2H, t, J= 6.0Hz), 5.46 (2H, brs), 6.18 (1H, s), 7.31 (1H, s)
[Work-example III-3] (composition of 5-********- 4-(3-chloro propoxy) methyl anthranilate)
2.02g (6.58mmmol) of 5-********- 4-(3-chloro propoxy)-2-nitroglycerine methyl benzoate and deployment Raney nickel 2.0g of 99% of the purity compounded in example IIIof reference-4 in the resisting pressure container of content volume 50mL, and methanol 40mL In addition, after replacing the inside of the system of reaction from hydrogen, it fastened, and it was made to react for 24 hours at hydrogen pressure 0.9MPa (gage pressure) and 90-100 degrees C. When reaction liquid was filtered after the end of a reaction and **** was analyzed by high speed liquid chromatography (absolutely determination method), 5-********- 4-(3-chloro propoxy) methyl anthranilate was generating 1.71g (reaction ****: 95.0%).
[Work-example III-4] (composition of 5-********- 4-(3-chloro propoxy) methyl anthranilate)
Churning equipment, a thermometer, a reflux condenser, and hydrogen gas 1.01g (3.29mmmol) of 5-********- 4-(3-chloro propoxy)-2-nitroglycerine methyl benzoate of 99% of the purity compounded in example IIIof reference-4 in the glass flasks of content volume 50mL equipped with the filled balloon, 3 mass % sulfuration platinum / 0.2g of carbon (65.7% water article), and methanol 40mL were added, and it was made to react at 40 degrees C in hydrogen atmosphere for 8 hours. When reaction liquid was filtered after the end of a reaction and **** was analyzed by high speed liquid chromatography (absolutely determination method), 5-********- 4-(3-chloro propoxy) methyl anthranilate was generating 0.88g (reaction ****: 98.0%).
[Work-example III-5] (composition of 5-********- 4-(3-chloro propoxy) methyl anthranilate)
Churning equipment, a thermometer, and a reflux condenser 1.01g (3.29mmmol) of 5-********- 4-(3-chloro propoxy)-2-nitroglycerine methyl benzoate of 99% of the purity compounded in example IIIof reference-4 in the glass flasks of content volume 50mL which it had, 10 mass % palladium / 0.5g of carbon, and Gyi acid 10mL were added, and it was made to react at 60 degrees C for 8 hours. When reaction liquid was filtered after the end of a reaction and **** was analyzed by high speed liquid chromatography (absolutely determination method), 5-********- 4-(3-chloro propoxy) methyl anthranilate was generating 0.78g (reaction ****: 87.0%). [Work-example III-6] (composition of 5-********- 4-(3-chloro propoxy) methyl anthranilate)
Churning equipment, a thermometer, and a reflux condenser 1.01g (3.29mmmol) of 5-********- 4-(3-chloro propoxy)-2-nitroglycerine methyl benzoate of 99% of the purity compounded in example IIIof reference-4 in the glass flasks of content volume 50mL which it had, Deployment Raney nickel 1.0g and Gyi acid 10mL were added, and it was made to react at 70 degrees C for 8 hours. When reaction liquid was filtered after the end of a reaction and **** was analyzed by high speed liquid chromatography (absolutely determination method), 5-********- 4-(3-chloro propoxy) methyl anthranilate was generating 0.77g (reaction ****: 85.0%).

[Work-example III-7] (composition of 5-********- 4-(3-chloro propoxy) methyl anthranilate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the reflux condenser, and the gas introduction pipe] 1.01g (3.29mmmol) of 5-********- 4-(3-chloro propoxy)-2-nitroglycerine methyl benzoate of 99% of the purity compounded in example IIIof reference-4, While adding 10 mass % palladium / 0.46g of carbon, and methanol 16mL and blowing hydrogen the speed for 50mL/under normal pressure It was made to react at 30 degrees C for 2 hours. When reaction liquid was filtered after the end of a reaction and **** was analyzed by high speed liquid chromatography (absolutely determination method), 5-********- 4-(3-chloro propoxy) methyl anthranilate was generating 0.85g (reaction ****: 95.2%).
[Example IIIof reference-5] (composition of 4-(3-bromo propoxy)-3-METOKISHI methyl benzoate)
It is 10.2g (54.9mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, the tap funnel, and the reflux condenser, 1, 3-dibromopropane 12.4g (60.4mmmol), 8.3g (60.4mmmol) of potassium carbonate, and acetonitrile 30mL are added, and it was made to react for 8 hours, agitating under flowing back (80-85 degrees C) in argon atmosphere. After the end of a reaction, after filtering reaction liquid, it condensed under decompression. A concentration thing is refined by silica gel column chromatography (bulking agent; WAKOGERU C-200, developing solvent; n-hexane), and it is a white crystal, 15.1g of 4-(3-bromo propoxy)-3-METOKISHI methyl benzoate of 98% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 88.8%).
The physical-properties value of 4-(3-bromo propoxy)-3-METOKISHI methyl benzoate was as follows.
Melting point; 65-66 degrees C
1H-NMR(CDCl3, delta (ppm));2.01-2.43 (2H, m), 3.61-3.65 (2H, m), 3.89 (3H, s), 3.93 (3H, s), 4.19 (2H, t, J= 6.0Hz), 6.90 (1H, d, J= 6.0Hz), 7.55 (1H, s), 7.67 (1H, d, J= 6.0Hz)
[Example IIIof reference-6] (composition of 5-********- 4-(3-bromo propoxy)-2-nitroglycerine methyl benzoate)
[the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 10.2g (33.0mmmol) of 4-(3-bromo propoxy)-3-METOKISHI methyl benzoate and 0.23g (3.30mmmol) of sodium nitrite of 98% of the purity compounded by example IIIof reference-5, and acetic acid 12.5mL. It heated. Subsequently, 13.8g (132.0mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at this temperature for 5 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing in order of water 30mL and n-Cheb Than 30mL, it is made to dry under decompression after filtering a crystal, and it is a white crystal, 10.7g of 5-********- 4-(3-bromo propoxy)-2-nitroglycerine methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 92.0%).
The physical-properties value of 5-********- 4-(3-bromo propoxy)-2-nitroglycerine methyl benzoate was as follows.

Melting point; 71-72 degrees C
1H-NMR(CDCl3, delta (ppm));2.37-2.45 (2H, m), 3.60-3.66 (2H, m), 3.90 (3H, s), 3.96 (3H, s), 7.08 (1H, s), 7.50 (1H, s)
[Work-example III-8] (composition of 5-********- 4-(3-bromo propoxy) methyl anthranilate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the reflux condenser, and the gas introduction pipe] It is 40 degrees C, adding and agitating 2.02g (5.75mmmol) of 5-********- 4-(3-bromo propoxy)-2-nitroglycerine methyl benzoate and methanol 40mL of 99% of purity which were compounded in example IIIof reference-6. It heated. Subsequently, it was made to react at this temperature for 2 hours, blowing hydrogen the speed for 50mL/under normal pressure, after adding 5 mass % palladium / 0.2g of carbon (49% water article) at this temperature. After the end of a reaction, when it condensed under decompression after filtering reaction liquid, the crystal deposited. It was made to dry under decompression of the obtained crystal, and 1.83g of 5-********- 4-(3-bromo propoxy) methyl anthranilate of 98% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 98.1%).
5-********- 4-(3-bromo propoxy) methyl anthranilate is a new compound shown with the following physical-properties values.
Melting point; 100-101 degrees C
1H-NMR(CDCl3, delta (ppm));2.34-2.43 (2H, m), 3.56-3.63 (2H, m), 3.75 (3H, s), 3.96 (3H, s), 5.55 (2H, brs), 6.18 (1H, s), 7.31 (1H, s)
[Example IIIof reference-7] (composition of 4-(3-chloro propoxy)-3-METOKISHI benzoic acid)
Churning equipment, a thermometer, and a tap funnel 18.2g (69.7mmmol) of 4-(3-chloro propoxy)-3-METOKISHI methyl benzoate of 99% of the purity compounded by the same method as example IIIof reference-3 in the glass flasks of content volume 300mL which it had, 2mol / L sodium hydroxide solution 69.7mL, and methanol 69.7mL were added, and it was made to react at 40 degrees C under argon atmosphere for 4 hours. After the end of a reaction, after cooling reaction liquid to 10 degrees C, when 2mol / L chloride 69.7mL was added and it neutralized, the crystal deposited. After filtering a crystal, it was made to dry under decompression, and 16.2g of 4-(3-chloro propoxy)-3-METOKISHI benzoic acid of 99% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 93.8%).
The physical-properties value of 4-(3-chloro propoxy)-3-METOKISHI benzoic acid was as follows.
Melting point; 150-152 degrees C
1H-NMR(CDCl3, delta (ppm));3.23-3.35 (2H, m), 3.68-3.88 (2H, m), 3.93 (3H, s), 4.35 (2H, t, J= 3.0Hz), 6.95 (1H, d, J= 6.0Hz), 7.57 (1H, s), 7.70 (1H, d, J= 6.0Hz)
[Example IIIof reference-8] (composition of 5-********- 4-(3-chloro propoxy)-2-nitroglycerine benzoic acid)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 16.2g (65.4mmmol) of 4-(3-chloro propoxy)-3-METOKISHI benzoic acid and 0.45g (6.54mmmol) of sodium nitrite of 98% of the purity compounded by example IIIof reference-7, and acetic acid 20mL. It heated. Subsequently, 27.6g (262.0mmmol) of 60

mass % nitric acid was dropped gently, and was made to react at this temperature for 5 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing by water 30mL, it was made to dry under decompression after filtering a crystal, and 17.9g of 5-********- 4-(3-chloro propoxy)-2-nitroglycerine benzoic acid of 99% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 93.0%).
The physical-properties value of 5-********- 4-(3-chloro propoxy)-2-nitroglycerine benzoic acid was as follows.
Melting point; 155-156 degrees C
1H-NMR(CDCl3, delta (ppm));2.37-2.45 (2H, m), 3.60-3.66 (2H, m), 3.90 (3H, s), 3.96 (3H, s), 7.08 (1H, s), 7.50 (1H, s)
[Work-example III-9] (composition of 5-********- 4-(3-chloro propoxy) anthranilic acid)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the reflux condenser, and the gas introduction pipe] It is 40 degrees C, adding and agitating 2.04g (6.90mmmol) of 5-********- 4-(3-chloro propoxy)-2-nitroglycerine benzoic acid and methanol 40mL of 99% of purity which were compounded in example IIIof reference-8. It heated. Subsequently, it was made to react at this temperature for 2 hours, blowing hydrogen the speed for 50mL/under normal pressure, after adding 5 mass % palladium / 0.2g of carbon (49% water article) at this temperature. After the end of a reaction, when it condensed under decompression after filtering reaction liquid, the crystal deposited. It was made to dry under decompression of the obtained crystal, and 1.83g of 5-********- 4-(3-chloro propoxy) anthranilic acid of 98% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 97.0%).
5-********- 4-(3-chloro propoxy) anthranilic acid is a new compound shown with the following physical-properties values.
Melting point; 164-165 degrees C
1H-NMR(CDCl3, delta (ppm));2.15-2.23 (2H, m), 3.60 (3H, s), 3.80-4.00 (2H, m), 4.04 (2H, t, J= 6.0Hz), 6.36 (1H, s), 7.15 (1H, s), 8.05 (2H, brs), 8.10 (1H, brs)
[Example IIIof reference-9] (composition of 4-(4-chloro butoxy)-3-METOKISHI methyl benzoate)
It is 10.2g (54.9mmmol) of 4-hydroxy 3-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, and the reflux condenser, 4-bromo 1-chloro butane 12.5g (71.4mmmol), 8.3g (60.4mmmol) of potassium carbonate, and acetonitrile 300mL are added, and it was made to react for 8 hours, agitating under flowing back (80-85 degrees C) in argon atmosphere. After the end of a reaction, after filtering reaction liquid, it condenses under decompression, and a concentration thing is refined by silica gel column chromatography (bulking agent; WAKOGERU C-200, developing solvent; n-hexane), and it is a colorless liquid, 13.6g of 4-(4-chloro butoxy)-3-METOKISHI methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 90.0%).
The physical-properties value of 4-(4-chloro butoxy)-3-METOKISHI methyl benzoate was as follows.
1H-NMR(CDCl3, delta (ppm));1.96-2.07 (4H, m), 3.61-3.67 (2H, m), 3.89 (3H, s), 3.93

(3H, s), 4.13 (2H, t, J= 6.0Hz), 6.87 (1H, d, J= 6.0Hz), 7.55 (1H, s), 7.64 (1H, d, J= 7Hz)
[Example IIIof reference-10] (composition of 5-********- 4-(4-chloro butoxy)-2-nitroglycerine methyl benzoate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 10.1g (36.7mmmol) of 4-(4-chloro butoxy)-3-METOKISHI methyl benzoate and 0.25g (3.67mmmol) of sodium nitrite of 99% of the purity compounded by example IIIof reference-9, and acetic acid 12.5mL. It heated. Subsequently, 115.4g (146.8mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at this temperature for 5 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing in order of water 30mL and n-Cheb Than 30mL, it is made to dry under decompression after filtering a crystal, and it is a white crystal, 10.9g of 5-********- 4-(4-chloro butoxy)-2-nitroglycerine methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 92.0%).
The physical-properties value of 5-********- 4-(4-chloro butoxy)-2-nitroglycerine methyl benzoate was as follows.
Melting point; 74-75 degrees C
1H-NMR(CDCl3, delta (ppm));1.95-2.10 (4H, m), 3.61-3.66 (2H, m), 3.89 (3H, s), 3.93 (3H, s), 4.13 (2H, t, J= 6.0Hz), 6.87 (1H, d, J= 6.0Hz), 7.26 (1H, s), 7.44 (1H, s)
[Work-example III-10] (composition of 5-********- 4-(4-chloro butoxy) methyl anthranilate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the reflux condenser, and the gas introduction pipe] It is 40 degrees C, adding and agitating 2.02g (6.29mmmol) of 5-********- 4-(4-chloro butoxy)-2-nitroglycerine methyl benzoate and methanol 40mL of 99% of purity which were compounded in example IIIof reference-10. It heated. Subsequently, it was made to react at this temperature for 2 hours, blowing hydrogen the speed for 50mL/under normal pressure, after adding 5 mass % palladium / 0.2g of carbon (49% water article) at this temperature. After the end of a reaction, when it condensed under decompression after filtering reaction liquid, the crystal deposited. It was made to dry under decompression of the obtained crystal, and 1.81g of 5-********- 4-(4-chloro butoxy) methyl anthranilate of 98% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 98.1%).
5-********- 4-(4-chloro butoxy) methyl anthranilate is a new compound shown with the following physical-properties values.
Melting point; 85-86 degrees C
1H-NMR(CDCl3, delta (ppm));1.92-2.90 (4H, m), 3.61-3.65 (2H, m), 3.76 (3H, s), 3.93 (3H, s), 4.03 (2H, t, J= 6.0Hz), 5.47 (2H, brs), 6.13 (1H, s), 7.31 (1H, s)
[Example IIIof reference-11] (composition of 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate)
It is 10.2g (54.9mmmol) of 3-hydroxy 4-METOKISHI methyl benzoate of purity 98 mass % to the glass flasks of content volume 100mL equipped with churning equipment, the thermometer, and the reflux condenser, 3-bromo 1-chloro propane 11.2g (71.4mmmol), 8.3g (60.4mmmol) of potassium carbonate, and acetone 30mL are added, and it was made to react for 8 hours, agitating under flowing back (80-85 degrees C) in argon

atmosphere. Reaction liquid was filtered after the end of a reaction, n-Cheb Than was added to the concentration thing, and the crystal was deposited. After filtering a crystal, it was made to dry under decompression, and 13.7g of 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 95.8%).
The physical-properties value of 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate was as follows.
Melting point; 46-48 degrees C
1H-NMR(CDCl3, delta (ppm));2.27-2.33 (2H, m), 3.64-3.75 (2H, m), 3.79 (3H, s), 3.91 (3H, s), 4.21 (2H, t, J= 5.0Hz), 6.88 (1H, d, J= 6.0Hz), 7.67 (1H, d, J= 6.0Hz), 7.58 (1H, s), 7.70 (1H, d, J= 6.0Hz)
[Example IIIof reference-12] (composition of 4-********- 5-(3-chloro propoxy)-2-nitroglycerine methyl benzoate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 10.1g (38.7mmmol) of 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate and 0.27g (3.87mmmol) of sodium nitrite of 99% of the purity compounded by example IIIof reference-11, and acetic acid 12.5mL. It heated. Subsequently, 16.2g (154.8mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at this temperature for 5 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing in order of water 30mL and n-Cheb Than 30mL, it is made to dry under decompression after filtering a crystal, and it is a white crystal, 11.3g of 4-********- 5-(3-chloro propoxy)-2-nitroglycerine methyl benzoate of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 95.0%).
The physical-properties value of 4-********- 5-(3-chloro propoxy)-2-nitroglycerine methyl benzoate was as follows.
Melting point; 63-64 degrees C
1H-NMR(CDCl3, delta (ppm));2.28-2.37 (2H, m), 3.64-3.75 (2H, m), 3.89 (3H, s), 3.99 (3H, s), 4.24 (2H, t, J= 5.0Hz), 7.11 (1H, s), 7.45 (1H, s)
[Work-example III-11] (composition of 4-********- 5-(3-chloro propoxy) methyl anthranilate)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the reflux condenser, and the gas introduction pipe] It is 40 degrees C, adding and agitating 2.02g (6.58mmmol) of 4-********- 5-(3-chloro propoxy)-2-nitroglycerine methyl benzoate and methanol 40mL of 99% of purity which were compounded in example IIIof reference-12. It heated. Subsequently, it was made to react at this temperature for 2 hours, blowing hydrogen the speed for 50mL/under normal pressure, after adding 5 mass % palladium / 0.2g of carbon (49% water article) at this temperature. After the end of a reaction, when it condensed under decompression after filtering reaction liquid, the crystal deposited. It was made to dry under decompression of the obtained crystal, and 1.80g of 4-********- 5-(3-chloro propoxy) methyl anthranilate of 98% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 98.1%).
The physical-properties value of 4-********- 5-(3-chloro propoxy) methyl anthranilate was as follows.

Melting point; 92-93 degrees C
1H-NMR(CDCl3, delta (ppm));2.19-2.27 (2H, m), 2.73-2.76 (2H, m), 3.80 (3H, s), 3.84 (3H, s), 4.09 (2H, t, J= 6.0Hz), 5.59 (2H, brs), 6.13 (1H, s), 7.37 (1H, s)
[Example IIIof reference-13] (composition of 3-(3-chloro propoxy)-4-METOKISHI benzoic acid)
Churning equipment, a thermometer, and a tap funnel 18.2g (69.7mmmol) of 3-(3-chloro propoxy)-4-METOKISHI methyl benzoate of 99% of the purity compounded by the same method as example IIIof reference-11 in the glass flasks of content volume 300mL which it had, 2mol / L sodium hydroxide solution 69.7mL, and methanol 69.7mL were added, and it was made to react at 40 degrees C under argon atmosphere for 4 hours. After the end of a reaction, after cooling reaction liquid to 10 degrees C, when 2mol / L chloride 69.7mL was added and it neutralized, the crystal deposited. After filtering a crystal, it is made to dry under decompression, and it is a white crystal (17.2g of 3-(3-chloro propoxy)-4-METOKISHI benzoic acid of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 95.8%).).
The physical-properties value of 3-(3-chloro propoxy)-4-METOKISHI benzoic acid was as follows.
Melting point; 152-153 degrees C
1H-NMR(CDCl3, delta (ppm));2.14-2.23 (2H, m), 3.64-3.75 (2H, m), 3.79 (3H, s), 3.91 (3H, s), 4.12 (2H, t, J= 5.0Hz), 7.04 (1H, d, J= 5.0Hz), 7.45 (1H, s), 7.70 (1H, d, J= 6.0Hz), 12.5 (1H, brs)
[Example IIIof reference-14] (composition of 4-********- 5-(3-chloro propoxy)-2-nitroglycerine benzoic acid)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the tap funnel] It is 40 degrees C, adding and agitating 9.57g (38.7mmmol) of 3-(3-chloro propoxy)-4-METOKISHI benzoic acid and 0.27g (3.87mmmol) of sodium nitrite of 99% of the purity compounded in example IIIof reference-13, and acetic acid 12.5mL. It heated. Subsequently, 16.2g (154.8mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at this temperature for 5 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing in order of water 30mL and n-Cheb Than 30mL, it is made to dry under decompression after filtering a crystal, and it is a white crystal, 10.4g of 4-********- 5-(3-chloro propoxy)-2-nitroglycerine benzoic acid of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 92.0%).
The physical-properties value of 4-********- 5-(3-chloro propoxy)-2-nitroglycerine benzoic acid was as follows.
Melting point; 162-163 degrees C
1H-NMR(CDCl3, delta (ppm));1.98-2.25 (2H, m), 3.65-3.75 (2H, m), 3.89 (3H, s), 3.94 (3H, s), 4.24 (2H, t, J= 5.0Hz), 7.33 (1H, s), 8.31 (1H, s), 13.5 (1H, brs)
[Work-example III-12] (composition of 4-********- 5-(3-chloro propoxy) anthranilic acid)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the reflux condenser, and the gas introduction pipe] It is 40 degrees C, adding and agitating 4.00g (13.5mmmol) of 4-********- 5-(3-chloro propoxy)-2-nitroglycerine benzoic acid and methanol 40mL of 99% of purity which were

compounded in example IIIof reference-14. It heated. Subsequently, it was made to react at this temperature for 4 hours, blowing hydrogen the speed for 50mL/under normal pressure, after adding 5 mass % palladium / 0.4g of carbon (49% water article) at this temperature. After the end of a reaction, when it condensed under decompression after filtering reaction liquid, the crystal deposited. It was made to dry under decompression of the obtained crystal, and 3.52g of 4-********- 5-(3-chloro propoxy) anthranilic acid of 98% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 98.1%).
4-********- 5-(3-chloro propoxy) anthranilic acid is a new compound shown with the following physical-properties values.
Melting point; 115-116 degrees C
1H-NMR(CDCl3, delta (ppm));2.05-2.13 (2H, m), 3.50 (3H, s), 3.74-3.90 (4H, m), 4.35 (2H, t, J= 6.0Hz), 6.30 (1H, s), 7.43 (1H, s), 8.30 (2H, brs), 8.32 (1H, brs)
[Example IIIof reference-15] (composition of 4-(2-chloroethoxy)-3-METOKISHI benzoic acid)
Churning equipment, a thermometer, and a tap funnel 17.40g (69.7mmmol) of 4-(2-chloroethoxy)-3-METOKISHI methyl benzoate of 98% of the purity compounded by the same method as example IIIof reference-1 in the glass flasks of content volume 300mL which it had, 2mol / L sodium hydroxide solution 69.7mL, and methanol 69.7mL were added, and it was made to react at 40 degrees C under argon atmosphere for 4 hours. After the end of a reaction, after cooling reaction liquid to 10 degrees C, 2mol / L chloride 69.7mL was added, and it neutralized. Subsequently, when methanol was made to distill off under decompression and reaction liquid was again cooled to 10 degrees C, the crystal deposited. It was made to dry under decompression after filtering a crystal, and 15.5g of 4-(2-chloroethoxy)-3-METOKISHI benzoic acid of 99% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 95.2%).
The physical-properties value of 4-(2-chloroethoxy)-3-METOKISHI benzoic acid was as follows.
Melting point; 205-206 degrees C
1H-NMR(DMSO-d6, delta (ppm));3.84 (3H, s), 3.93-4.01 (2H, m), 4.31-4.33 (2H, m), 7.06 (1H, s), 7.47 (1H, s), 7.55 (1H, s), 12.73 (1H, brs)
[Example IIIof reference-16] (composition of 5-********- 4-(2-chloroethoxy)-2-nitroglycerine benzoic acid)
[the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, and the tap funnel] It is 50 degrees C, adding and agitating 9.0g (38.7mmmol) of 4-(2-chloroethoxy)-3-METOKISHI benzoic acid and 0.27g (3.87mmmol) of sodium nitrite of 99% of the purity compounded by example IIIof reference-15, and acetic acid 12.5mL. It heated. Subsequently, 16.2g (154.8mmmol) of 60 mass % nitric acid was dropped gently, and was made to react at this temperature for 10 hours. After the end of a reaction, when water 20mL was added and it cooled to 20 degrees C, the crystal deposited. After washing in order of water 30mL and n-Cheb Than 30mL, it is made to dry under decompression after filtering a crystal, and it is a white crystal, 9.91g of 5-********- 4-(2-chloroethoxy)-2-nitroglycerine benzoic acid of 99% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 92.0%).

The physical-properties value of 5-********- 4-(2-chloroethoxy)-2-nitroglycerine benzoic acid was as follows.
Melting point; 172-173 degrees C
1H-NMR(DMSO-d6, delta (ppm));3.91 (3H, s), 3.93-4.01 (2H, m), 4.41-4.47 (2H, m), 7.33 (1H, s), 7.61 (1H, s), 13.6 (1H, brs).
[Work-example III-13] (composition of 5-********- 4-(2-chloroethoxy) anthranilic acid) [the glass flasks of content volume 50mL equipped with churning equipment, the thermometer, the reflux condenser, and the gas introduction pipe] It is 40 degrees C, agitating, after adding 3.76g (13.5mmmol) of 5-********- 4-(2-chloroethoxy)-2-nitroglycerine benzoic acid and methanol 40mL of 99% of the purity compounded in example IIIof reference-16, and 0.4g of 5 mass % palladium / carbon (49% water article). It heated. Subsequently, it was made to react at this temperature for 4 hours, blowing hydrogen the speed for 50mL/under normal pressure. After the end of a reaction, when it condensed under decompression after filtering reaction liquid, the crystal deposited. It was made to dry under decompression of the obtained crystal, and 3.27g of 5-********- 4-(2-chloroethoxy) anthranilic acid of 99% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 98.1%).
5-********- 4-(2-chloroethoxy) anthranilic acid is a new compound shown with the following physical-properties values.
Melting point; 182-183 degrees C
1H-NMR(DMSO-d6, delta (ppm));3.70 (3H, s), 3.93-3.97 (2H, m), 4.18-4.21 (2H, m), 6.31 (1H, s), 7.15 (1H, s), 8.31 (2H, brs), 8.35 (1H, brs)
[Work-example IV-1] (composition of 6-********- 7-(3-chloro propoxy) quinazoline 4-ON)
Churning equipment, a thermometer, and a pressure gauge In the resisting pressure container made from stainless steel of content volume 1000mL which it had, 161.5g (0.59mol) of 5-********- 4-(3-chloro propoxy) methyl anthranilate, ORUTOGI acid MECHIRU 156.5g (1.48mol), 113.7g (1.48mol) of ammonium acetate, and methanol 300mL were added, and it fastened, and was made to react at 90-95 degrees C for 8 hours. The pressure in that case was 0.1 - 0.3mpa (gage pressure). Since the crystal deposited when water 600mL is added after the end of a reaction and it was made to agitate at 0-10 degrees C for 1 hour, it filtered. The obtained crystal was dried at 60 degrees C under decompression after washing by water 600mL, and the 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 152.8g was obtained as a white crystal (isolation ****: 94%).
In addition, 6-********- 7-(3-chloro propoxy) quinazoline 4-ON is a new compound shown with the following physical-properties values.
Melting point; 259 degrees C
CI-MS(m/e);269(M+1)
1H-NMR(DMSO-d6, delta (ppm));2.19-2.28 (2H, m), 3.80 (2H, t, J= 6.6Hz), 3.88 (3H, s), 4.24 (2H, t, J= 6.0Hz), 7.16 (1H, s), 7.46 (1H, s), 7.99 (1H, s), 11.0 (1H, brs)
13C-NMR(DMSO-d6, delta (ppm));31.4, 41.8, 55.7, 65.2, 105.1, 108.7, 115.7, 143.8, 144.7, 148.5, 153.4, 160.0
Ultimate analysis; 53.41% of carbon, 4.90% of hydrogen, 10.05% of nitrogen (Theoretical value (C12H13ClN2O3); 53.64% of carbon, 4.88% of hydrogen, 10.43% of nitrogen)

[Work-example IV-2] (composition of 7-********- 6-(3-chloro propoxy) quinazoline 4-ON)
Churning equipment and a thermometer In the resisting pressure container made from stainless steel of content volume 10mL which it had, 1.0g (3.7mmmol) of 4-********- 5-(3-chloro propoxy) methyl anthranilate, ORUTOGI acid MECHIRU 0.93g (8.8mmmol), 0.67g (8.8mmmol) of ammonium acetate, and methanol 5mL were added, and it fastened, and was made to react at 90-95 degrees C for 8 hours. Since the crystal deposited when water 50mL is added after the end of a reaction and it was made to agitate at 25 degrees C for 1 hour, it filtered. The obtained crystal was dried at 60 degrees C under decompression, and the 7-********- 6-(3-chloro propoxy) quinazoline 4-ON 0.89g was obtained as a white crystal (isolation ****: 91%).
In addition, 7-********- 6-(3-chloro propoxy) quinazoline 4-ON is a new compound shown with the following physical-properties values.
CI-MS(m/e);269(M+1)
1H-NMR(DMSO-d6, delta (ppm));2.19-2.72 (2H, m), 3.80 (2H, t, J= 6.6Hz), 3.91 (3H, s), 4.19 (2H, t, J= 6.0Hz), 7.15 (1H, s), 7.47 (1H, s), 7.99 (1H, s), 11.0 (1H, brs)
[Work-example IV-3] (composition of 6-********- 7-(2-chloroethoxy) quinazoline 4-ON)
Churning equipment and a thermometer In the resisting pressure container made from stainless steel of content volume 10mL which it had, 1.0g (3.9mmmol) of 5-********- 4-(2-chloroethoxy) methyl anthranilate, ORUTOGI acid MECHIRU 1.02g (9.6mmmol), 0.74g (9.6mmmol) of ammonium acetate, and methanol 5mL were added, and it fastened, and was made to react at 90-95 degrees C for 8 hours. Since the crystal deposited when water 50mL is added after the end of a reaction and it was made to agitate at 25 degrees C for 1 hour, it filtered. The obtained crystal was dried at 60 degrees C under decompression, and the 6-********- 7-(2-chloroethoxy) quinazoline 4-ON 0.87g was obtained as a gray crystal (isolation ****: 89%).
In addition, 6-********- 7-(2-chloroethoxy) quinazoline 4-ON is a new compound shown with the following physical-properties values.
CI-MS(m/e);255(M+1)
1H-NMR(DMSO-d6, delta (ppm));3.89 (3H, s), 4.01 (2H, t, J= 5.5Hz), 4.41 (2H, t, J= 5.5Hz), 7.16 (1H, s), 7.47 (1H, s), 7.99 (1H, s), 11.0 (1H, brs)
[Work-example IV-4] (composition of 6-********- 7-(4-chloro butoxy) quinazoline 4-ON)
Churning equipment and a thermometer In the resisting pressure container made from stainless steel of content volume 10mL which it had, 1.1g (3.5mmmol) of 5-********- 4-(4-chloro butoxy) methyl anthranilate, ORUTOGI acid MECHIRU 0.92g (8.8mmmol), 0.67g (8.8mmmol) of ammonium acetate, and methanol 5mL were added, and it fastened, and was made to react at 90-95 degrees C for 8 hours. Since the crystal deposited when water 50mL is added after the end of a reaction and it was made to agitate at 25 degrees C for 1 hour, it filtered. The obtained crystal was dried at 60 degrees C under decompression, and the 6-********- 7-(4-chloro butoxy) quinazoline 4-ON 0.94g was obtained as a gray crystal (isolation ****: 96%).
In addition, 6-********- 7-(4-chloro butoxy) quinazoline 4-ON is a new compound shown with the following physical-properties values.
CI-MS(m/e);283(M+1)

1H-NMR(DMSO-d6, delta (ppm));1.88-1.92 (4H, m), 3.72-3.76 (2H, m), 3.87 (3H, s), 4.13-4.15 (2H, m), 7.14 (1H, s), 7.44 (1H, s), 7.98 (1H, s), 12.1 (1H, brs)
[The example V-1 of reference] (composition of 6-********- 7-(3-chloro propoxy) quinazoline 4-ON)
Churning equipment, a thermometer, and a pressure gauge In the resisting pressure container made from stainless steel of content volume 1000mL which it had, 161.5g (0.59mol) of 5-********- 4-(3-chloro propoxy) methyl anthranilate, ORUTOGI acid MECHIRU 156.5g (1.48mol), 113.7g (1.48mol) of ammonium acetate, and methanol 300mL were added, and it fastened, and was made to react at 90-95 degrees C for 8 hours. The pressure in that case was 0.1 - 0.3mpa (gage pressure). Since the crystal deposited when water 600mL is added after the end of a reaction and it was made to agitate at 0-10 degrees C for 1 hour, it filtered. The obtained crystal was dried at 60 degrees C under decompression after washing by water 600mL, and the 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 152.8g was obtained as a white crystal (isolation ****: 94%).
In addition, the physical-properties value of 6-********- 7-(3-chloro propoxy) quinazoline 4-ON was as follows.
Melting point; 259 degrees C
CI-MS(m/e);269(M+1)
1H-NMR(DMSO-d6, delta (ppm));2.19-2.28 (2H, m), 3.80 (2H, t, J= 6.6Hz), 3.88 (3H, s), 4.24 (2H, t, J= 6.0Hz), 7.16 (1H, s), 7.46 (1H, s), 7.99 (1H, s), 11.0 (1H, brs)
13C-NMR(DMSO-d6, delta (ppm));31.4, 41.8, 55.7, 65.2, 105.1, 108.7, 115.7, 143.8, 144.7, 148.5, 153.4, 160.0
Ultimate analysis; 53.41% of carbon, 4.90% of hydrogen, 10.05% of nitrogen (Theoretical value (C12H13ClN2O3); 53.64% of carbon, 4.88% of hydrogen, 10.43% of nitrogen)
[Work example V-1] (composition of 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON)
Make it be the same as that of the method of the example V-1 of reference in the glass containers of content volume 500mL equipped with churning equipment, the thermometer, and the reflux condenser. It was made to react at 105 degrees C for 18 hours, adding and agitating the 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 95.0g (0.354mol), compound MORUHORIN 154.2g (1.77mol), and compound sec-butyl alcohol 380mL. After the end of a reaction, after adding methanol 380mL and agitating for 30 minutes at 70 degrees C, subsequently, reaction liquid was cooled to room temperature and it agitated for 30 minutes at room temperature. After filtering again, it is made to dry at 60 degrees C under decompression after washing after filtering the crystal which deposited, agitating in addition to methanol 190mL, and it is a white crystal. The 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON 104g of 98.81% (area percentage by high speed liquid chromatography) of purity was obtained (isolation ****: 92%).
In addition, the physical-properties value of 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON was as follows.
CI-MS(m/e);320(M+1)
1H-NMR(DMSO-d6, delta (ppm));2.08-2.13 (2H, m), 2.48 (4H, t, J= 4.5Hz), 2.56 (2H, t, J= 6.9Hz), 3.73 (4H, t, J= 4.5Hz), 4.00 (3H, s), 4.24 (2H, t, J= 6.6Hz), 7.18 (1H, s), 7.60

(1H, s), 8.02 (1H, s), 10.5 (1H, brs)
Ultimate analysis; 59.71% of carbon, 6.62% of hydrogen, 13.10% of nitrogen (Theoretical value (C16H21N3O4); 60.17% of carbon, 6.63% of hydrogen, 13.16% of nitrogen)
[Work example V-2] (composition of 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON chloride salt)
[the glass containers of content volume 1000mL equipped with churning equipment, the thermometer, and the reflux condenser] While adding and agitating the 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON 90g (0.284mol), 12mol / L chloride 94mL (1.13mol), and methanol 180mL which were compounded by the same method as a work example V-1 It was made to react at room temperature for 1 hour. After the end of a reaction, acetone 360mL was added to reaction liquid, and it cooled to 5 degrees C, and agitated for 1 hour. The crystal which deposited was filtered and 113g of rough crystals of the 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON chloride salt of 99.16% (area percentage by high speed liquid chromatography) of purity were obtained. Furthermore, 105g of this rough crystal and methanol 700mL were mixed, and it was made to agitate at 60 degrees C for 1 hour. Cooled to room temperature after the end of churning, filtered the crystal which deposited, it was made to dry under decompression, and 98g of 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON chloride salt of 99.74% (area percentage by high speed liquid chromatography) of purity was obtained.
[Work example V-3] (composition of 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON)
Make it be the same as that of the method of the example V-1 of reference in the glass containers of content volume 25mL equipped with churning equipment, the thermometer, and the reflux condenser. It was made to react at 105 degrees C for 4 hours, adding and agitating the compound 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 2.0g (7.4mmmol) and compound MORUHORIN 6.45g (74mmmol). After the end of a reaction, when reaction liquid was analyzed by high speed liquid chromatography (absolutely analytical curve method), 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON was generating 2.17g (reaction ****: 92%).
[Work example V-4] (composition of 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON)
Make it be the same as that of the method of the example V-1 of reference in the resisting pressure container made from stainless steel of content volume 10mL equipped with churning equipment and a thermometer. It was made to react at 105 degrees C for 4 hours, adding and agitating the 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 1.0g (3.7mmmol), compound MORUHORIN 1.61g (18.5mmmol), and compound methanol 4mL. After the end of a reaction, when reaction liquid was analyzed by high speed liquid chromatography (absolutely analytical curve method), 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON was generating 1.10g (reaction ****: 93%).
[Work example V-5] (composition of 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON)
Make it be the same as that of the method of the example V-1 of reference in the glass containers of content volume 5mL equipped with churning equipment and a thermometer. The 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 0.5g (1.9mmmol), compound MORUHORIN 0.5g (5.7mmmol), and compound 4.0mol / L sodium hydroxide solution

1.0mL (4.0mmmol) is added. It was made to react at 50 degrees C for 2 hours, agitating. After the end of a reaction, when reaction liquid was analyzed by high speed liquid chromatography (absolutely analytical curve method), 6-********- 7-(3-morpholino propoxy) quinazoline 4-ON was generating 0.57g (reaction ****: 94%).

[Work example V-6] (composition of 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON)

Make it be the same as that of the method of the example V-1 of reference in the glass containers of content volume 100mL equipped with churning equipment and a thermometer. The compound 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 15.0g (55.8mmmol), It was made to react at 55 degrees C for 5 hours, adding and agitating PIPERIJIN 13.85g (163mmmol), and 4.0mol / L sodium hydroxide solution 28.4mL (113.6mmmol). After the end of a reaction, after cooling reaction liquid to room temperature, unreacted PIPERIJIN was distilled off under decompression, and subsequently, 6.0mol / L chloride 18.9mL (113.4mmmol) was added, and it cooled to 0 degree C. Filtered the crystal which deposited, it was made to dry at 60 degrees C under decompression, and the 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON 13.5g was obtained as a white crystal (isolation ****: 76.3%).

In addition, the physical-properties value of 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON was as follows.

CI-MS(m/e);318(M+1)

1H-NMR(DMSO-d6, delta (ppm));1.45-1.47 (2H, m), 1.62 (4H, t, J= 6.0Hz), 2.10-2.14 (2H, m), 2.42-2.48 (4H, m), 2.57 (2H, t, J= 6.6Hz), 3.99 (3H, s), 4.21 (2H, t, J= 6.3Hz), 7.10 (1H, s), 7.56 (1H, s), 7.98 (1H, s), 10.5 (1H, brs)

[Work example V-7] (composition of 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON)

[the glass containers of content volume 5mL equipped with churning equipment and a thermometer] The 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 0.5g (1.9mmmol), PIPERIJIN 0.81g (9.5mmmol), and 4.0mol / L sodium hydroxide solution 4.8mL (19mmmol) which was the same as that of the method of the example V-1 of reference, and was compounded is added. While agitating It was made to react at 50 degrees C for 5 hours. After the end of a reaction, when reaction liquid was analyzed by high speed liquid chromatography (absolutely analytical curve method), 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON was generating 0.51g (reaction ****: 85%).

[Work example V-8] (composition of 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON)

Make it be the same as that of the method of the example V-1 of reference in the glass containers of content volume 5mL equipped with churning equipment and a thermometer. The 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 1.0g (3.7mmmol), compound PIPERIJIN 0.48g (5.6mmmol), and compound 4.0mol / L sodium hydroxide solution 4.8mL (19mmmol) is added. It was made to react at 50 degrees C for 5 hours, agitating. After the end of a reaction, when reaction liquid was analyzed by high speed liquid chromatography (absolutely analytical curve method), 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON was generating 1.05g (reaction ****: 89%).

[Work example V-9] (composition of 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON)

Make it be the same as that of the method of the example V-1 of reference in the glass

containers of content volume 5mL equipped with churning equipment and a thermometer. It was made to react at 80 degrees C for 5 hours, adding and agitating the 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 1.0g (3.7mmmol), compound PIPERIJIN 1.62g (19mmmol), and compound ethanol 10mL. After the end of a reaction, when reaction liquid was analyzed by high speed liquid chromatography (absolutely analytical curve method), 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON was generating 1.02g (reaction ****: 87%).

[Work example V-10] (composition of 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON)

Make it be the same as that of the method of the example V-1 of reference in the glass containers of content volume 5mL equipped with churning equipment and a thermometer. It was made to react at 105 degrees C for 5 hours, adding and agitating the 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 1.0g (3.7mmmol), compound PIPERIJIN 1.62g (19mmmol), and compound sec-butyl alcohol 10mL. After the end of a reaction, when reaction liquid was analyzed by high speed liquid chromatography (absolutely analytical curve method), 6-********- 7-(3-piperidino propoxy) quinazoline 4-ON was generating 1.06g (reaction ****: 90%).

[Work example V-11] (composition of 6-********- 7-(3-thiomorpholino propoxy) quinazoline 4-ON)

Make it be the same as that of the method of the example V-1 of reference in the glass containers of content volume 100mL equipped with churning equipment, the thermometer, and the reflux condenser. It was made to react at 105 degrees C for 7.5 hours, adding and agitating the 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 4.0g (14.9mmmol), compound CHIOMORUHORIN 5.0g (48.5mmmol), and compound sec-butyl alcohol 16mL. After the end of a reaction, after adding methanol 16mL to reaction liquid and flowing back for 1 hour, it cooled to room temperature. Filtered the crystal which deposited, it was made to dry at 60 degrees C under decompression, and the 6-********- 7-(3-thiomorpholino propoxy) quinazoline 4-ON 4.38g of 92% (area percentage by high speed liquid chromatography) of purity was obtained as a white crystal (isolation ****: 81%).

In addition, 6-********- 7-(3-thiomorpholino propoxy) quinazoline 4-ON was a new compound shown with the following physical-properties values.

CI-MS(m/e);336(M+1)

1H-NMR(DMSO-d6, delta (ppm));1.87-1.96 (2H, m), 2.44-2.52 (2H, m), 2.59-2.66 (8H, m), 3.87 (3H, s), 4.14 (2H, t, J= 6.3Hz), 7.12 (1H, s), 7.44 (1H, s), 7.98 (1H, s), 12.0 (1H, brs)

[Work example V-12] (composition of 6-********- 7-[3-(2-MECHIRU piperidino propoxy)] quinazoline 4-ON)

Make it be the same as that of the method of the example V-1 of reference in the glass containers of content volume 100mL equipped with churning equipment, the thermometer, and the reflux condenser. The compound 6-********- 7-(3-chloro propoxy) quinazoline 4-ON 19.6g (73mmmol), It was made to react at 90-100 degrees C for 14 hours, adding and agitating 2-MECHIRUPIPE lysine 36.17g (365mmmol), 1-******- 2-pyrrolidinone 9.8mL (101.6mmmol), and sec-butyl alcohol 79mL. After the end of a reaction, methanol 80mL was added to reaction liquid, it agitated for 30 minutes at 60-70 degrees C, and, subsequently reaction liquid was agitated for 30 minutes at 0-10

degrees C. It washed by acetone 60mL after filtering the crystal which deposited, this crystal was dissolved in 1mol / L sodium hydroxide solution 118mL, and it agitated at 47 degrees C for 3 hours. After filtering again and adding to **** in order of water 36mL, 1-******- 2-pyrrolidinone 60mL, and 60mol / L chloride 18.7mL, it agitated for 30 minutes at 0-10 degrees C. The crystal which deposited was filtered, and this crystal was added to the mixed-solution of acetone 118mL and water 118mL, and, subsequently was agitated for 30 minutes at 20-30 degrees C at 50-60 degrees C for 1 hour. It was made to dry under decompression of output after filtration, and the 6-********- 7-[3-(2-MECHIRU piperidino propoxy)] quinazoline 4-ON 17.0g of 98.7% (area percentage by high speed liquid chromatography) of purity was obtained as a white solid (isolation ****: 69%).

In addition, the physical-properties value of 6-********- 7-[3-(2-MECHIRU piperidino propoxy)] quinazoline 4-ON was as follows.

CI-MS(m/e);332(M+1)

1H-NMR(DMSO-d6, delta (ppm));0.97 (3H, d, J= 6.0Hz), 1.02-1.30 (2H, m), 1.36-1.59 (4H, m), 1.72-1.91 (2H, m), 2.04-2.13 (1H, m), 2.24-2.39 (2H, m), 2.75-2.84 (2H, m), 3.86 (3H, s), 4.13 (2H, t, J= 6.3Hz), 7.11 (1H, s), 7.44 (1H, s), 7.97 (1H, s), 12.0 (1H, brs)

[Work example V-13] (composition of 6-********- 7-[3-(4-MECHIRU piperidino propoxy)] quinazoline 4-ON)

In the work example V-12, it experimented like the work example V-12 except having changed 2-MECHIRUPIPE lysine into 4-MECHIRUPIPE lysine.

As a result, the 6-********- 7-[3-(4-MECHIRU piperidino propoxy)] quinazoline 4-ON 21.3g of 99.5% (area percentage by high speed liquid chromatography) of purity was obtained as a white solid (isolation ****: 87%).

In addition, the physical-properties value of 6-********- 7-[3-(4-MECHIRU piperidino propoxy)] quinazoline 4-ON was as follows.

CI-MS(m/e);332(M+1)

1H-NMR(DMSO-d6, delta (ppm));0.88 (3H, d, J= 6.0Hz), 1.04-1.19 (2H, m), 1.27-1.34 (1H, m), 1.54-1.58 (2H, m), 1.81-1.95 (4H, m), 2.37-2.42 (2H, m), 2.80-2.84 (2H, m), 3.87 (3H, s), 4.11-4.15 (2H, m), 7.10 (1H, s), 7.44 (1H, s), 7.97 (1H, s), 12.0 (1H, brs)

[Industrial availability]

The suitable process for the industrial target which can manufacture under mild conditions by this invention, and can manufacture a quinazoline 4-ON derivative useful as synthetic intermediate of medicine or agricultural chemicals by quantity **** from an anthranilic acid derivative by a simple method can be offered. Moreover, various compounds useful as synthetic intermediate of medicine or agricultural chemicals can manufacture by an advantageous method industrially by this invention.